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DIET AND CORONARY DISEASE

J. B. DUGUID
M.D. Aberd.
PROFESSOR OF PATHOLOGY IN THE UNIVERSITY OF DURHAM

THE prevalence of coronary thrombosis in recent years has revived interest in the problem of atherosclerosis, and the question of diet as a factor is now receiving a great deal of attention. We have been so impressed by the fact that arterial lesions can be produced in animals by adding cholesterol to their food that we have been disposed to accept the diet hypothesis almost without question, and to infer from it that fatty foods are a cause of coronary disease. Nevertheless the incidence of coronary disease did not seem to decline in this country during the war when our intake of fats was restricted; nor, for that matter, do rabbits with cholesterol lesions tend to die from coronary thrombosis.

In connecting coronary disease with diet we have, I think, oversimplified the problem and taken too much for granted. We have assumed that atherosclerosis represents a single disease process referable to some particular combination of causes, whereas it can now be shown that lesions which go by that name may be the outcome of at least two different processes, with causes which may be quite unrelated to one another. This point, although mentioned as a possibility by White and Ferrero (1949) and by Shillingford (1952), has never been clearly brought out; but unless it is taken into account it is hardly possible to judge where diet may come into the picture. Let us compare, for example, the common form of coronary atherosclerosis with the lesions produced in rabbits by cholesterol feeding. Here I shall repeat, with fresh materials, a demonstration already made (Duguid 1946), because it illustrates certain principles which must be kept clearly in mind.

Coronary Atherosclerosis

The term atherosclerosis refers to a lesion of variable morphology but with two essential characters—namely, fatty change and fibrous thickening of the intima. Sometimes the one character is predominant and sometimes the other; but, in the form of coronary disease with which we are mainly concerned, fibrous thickening is the outstanding one, involving, as it often does, extreme narrowing of the vessel; and this, as I shall show, is a feature of crucial significance.

When the coronary arteries from cases of long-standing cardiac infarction are examined, occasional examples of canalised thrombi are found in which the affected vessels have two or more channels instead of a single lumen (fig. 1). In these it will often be noted that the fibrous tissue which separates the channels, and which obviously represents organised thrombus, merges with the intima so that the two are indistinguishable. Further, if serial sections are made, a point is reached where the channels unite to form a single lumen; and there it is found that the same organised thrombus extends along the vessel as an inner lining which looks like a fibrous overgrowth of the intima (fig. 2). The thrombus has in fact become part of the intima, and the appearance is that of a thickened artery.

The same thing happens with mural thrombi, which are much commoner than these producing total occlusion. When a mural thrombus forms in an artery it becomes covered with endothelium so that it is incorporated in the vessel wall, with the result that when it is subsequently organised it forms a fibrous thickening of the intima. Since most mural thrombi, before being completely organised, undergo fatty degeneration—sometimes with atheromatous softening and ulceration—they acquire all the characters of atherosclerotic plaques, and we thus learn that some of the lesions we classify as atherosclerosis are in fact organised, or partly organised, mural thrombi. It should of course be understood that most mural thrombi are very small, consisting of no more than microscopic layers of fibrin; but these, when laid down repeatedly one on top of another, can give rise to considerable thickenings of the vessel walls; and this appears to be the sequence of events in many examples of atherosclerosis.

These observations have now been confirmed in one way or another by a number of observers including Harrison (1948), Heard (1952), Geiringer (1951), McLetchie (1952), and Crawford and Levene (1952), and we may safely take it that thrombosis is one factor in the pathogenesis of atherosclerosis. That this has been overlooked in the past is due, I think, largely to the presence of fatty changes. We have not been accustomed to associate these with thrombosis, and their presence has prevented us from recognising the thrombi as such.

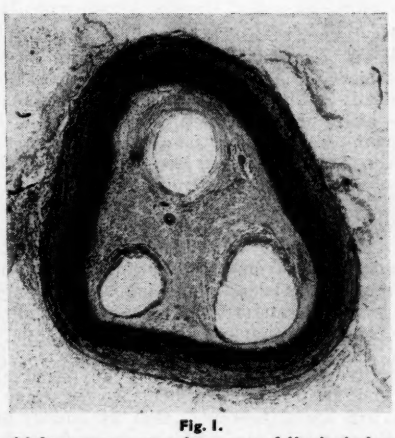

Fig. 1.

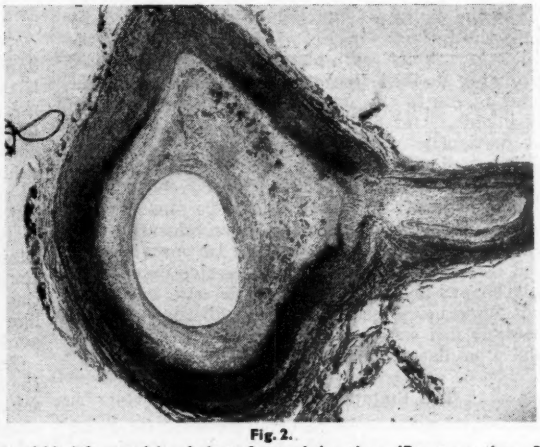

Fig. 2.

Canalised left coronary artery from man of 61 who had an infarct of his left ventricle of about 2 years' duration. (Frozen section: Sudan IV and haemalum. × 12.)

In fig. 1 the lumen is occupied by a mass of fibrous tissue which represents an organised thrombus with three separate channels.

In fig. 2, from a point less than 1 mm. distant, the channels have joined to form a single lumen while the thrombus now appears as a fibrous thickening of the wall.

Nevertheless fatty changes can be shown to be an almost constant feature of mural thrombi, not only in the arteries but in the heart, including endocardial vegetations, and "in venous thrombi of all kinds," as Cohnheim long ago remarked. The fats, which vary in amount, are presumably derived from the lipids present in the blood when the thrombi are formed.

Cholesterol Sclerosis in Rabbits

It is generally assumed that arterial thrombosis depends on some underlying lesion of the vessel wall, and a common example in the larger arteries is fatty change. To see whether cholesterol lesions would lead to thrombosis in rabbits Dr. I. Rannie and I have recently repeated the classical feeding experiments and studied the lesions in various stages of development. Rabbits were given 1·5 grammes of cholesterol daily in addition to their ordinary diet and killed after periods ranging from six weeks to more than a year. No mural thrombi were found, but much useful information was obtained from the experiments.

By the end of the sixth week there were changes in the aorta and pulmonary arteries consisting of small deposits of cholesterol-bearing phagocytes (foam cells) in the subendothelial layer of the intima, chiefly near the openings of branches. By the twentieth week the lesions were usually widespread and severe, with great accumulations of foam cells in the intima, often swelling the vessel wall to many times its normal thickness. In the superficial zones the foam cells were deposited in layers of variable thickness, with layers of spindle cells between forming a kind of stroma. In the deeper zones there was often complete disorganisation, the foam cells having disintegrated, leaving atheromatous masses of cholesterol and other fatty debris in their place. In rabbits allowed to survive more than a year the cholesterol had mostly disappeared, leaving dense fibrous thickenings of the intima, so that the condition could with every justification be termed atherosclerosis.

Our findings (Rannie and Duguid 1953) agree in general with those of other observers, but our interpretation embodies a somewhat unorthodox conception. It should be explained that authorities have differed in their views on the process by which cholesterol gets into the walls of the arteries. Duff (1936) and Hueper (1944) believed that it is precipitated from the tissue fluids and taken up by the intimal phagocytes, whilst Altschul (1950) thought that it is absorbed from the circulating blood into the lining endothelial cells and carried by them into the intima. In 1941 Leary put forward the view that in rabbits with hypercholesteræmia foam cells, probably derived from the liver, circulate in the blood and adhere to the arterial walls, which they then actively invade. Our findings supported this in all but the last particular. We saw convincing evidence that the cells in question were present in the blood and adhered to the vessel walls, but we came to the conclusion that instead of invading these, they simply become covered with endothelium and were thus passively incorporated in the same way as mural thrombi. In our view the advanced lesions were formed by successive deposits of foam cells heaped one on top of the other, with occasional layers of endothelial cells laid down between. The atheromatous foci were produced by the breakdown of older and more deeply buried deposits.

The Endothelial Reaction

The important point to be gathered from the foregoing comparative study is that atherosclerosis can arise by two different processes; mural thrombosis on the one hand, and the deposition of lipids, or lipid-bearing cells on the other. This alone should make us cautious in assigning causes. Two further points are I think worth recording although they are contingent on our own interpretation. The first is that in both processes the mechanism, in so far as the arteries are concerned, is the same; solid matter is deposited on the intimal surface and in due course covered with endothelium and incorporated in the intima. That this is a natural reaction of arteries to the presence of solids in their lumen can be shown by inserting a silk thread into the femoral artery of a dog. The thread becomes fixed to the intimal surface with fibrin and the whole mass covered with endothelium and organised, so as to produce a fair imitation of an atherosclerotic nodule (fig. 3) but with silk instead of fat in its centre. The reaction provides an effective means of disposal of undesirable solids from the blood-stream.

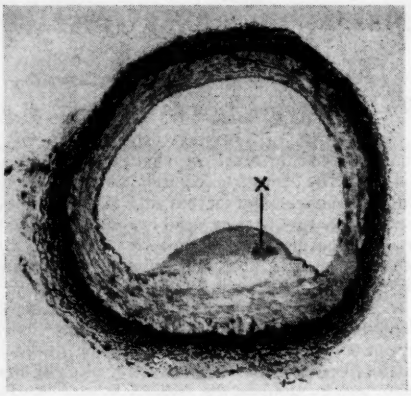

Fig. 3—Dog's femoral artery into which a silk thread (x) has been inserted and then passed down the lumen. The thread is surrounded by organised thrombus which has been incorporated in the intima to form a fibrous thickening. (Paraffin section: Weigert's elastic tissue stain. × 20.)

The second point is that in none of the processes are the thickenings the result of changes in the original tissues of the vessel wall, as visualised in the current conception of atherosclerosis. All are products of substances deposited on the intimal surface; and thus, if our interpretations are correct, we may take it that atherosclerosis is not a specific disease but merely the common end-result of a number of different pathological processes with different causes.

The Pathogenesis of Human Atherosclerosis

The development of cholesterol lesions has been demonstrated in rabbits, but there is reason to believe that something of the same kind occurs in man, although not necessarily as a result of diet. The "xanthomatous" deposits which appear in the arteries in familial hypercholesteræmia are probably the exact counterpart of the rabbit lesion, but they are too rare to be of much account in the pathology of atherosclerosis. A much commoner lesion of similar morphology is the so-called superficial fatty streaking which occurs in the aortas of young subjects. This consists of deposits of fat-laden cells in the subendothelial layers of the intima, chiefly around the openings of branches, producing an appearance so like the early cholesterol lesions that it is difficult to avoid the conclusion that the same process is involved.

Similar changes are seen in older subjects; but in them they tend to be obscured by advanced atherosclerosis and are therefore difficult to interpret. All observers will agree, however, that in human atherosclerosis changes take place which cannot be put down to thrombosis; and some of them, we may suppose, are of a primary fatty nature, analogous to the cholesterol lesions of rabbits.

Thus we may take it that in man there are two pathogenetically distinct forms of atherosclerosis, and

before arriving at any conclusions as to causation we must have some means of distinguishing them and assessing their relative incidence. Unfortunately most of the lesions we find in human arteries are of long standing, and have passed through a succession of changes which obscures their origin; but sometimes certain distinguishing features persist, and one of them is narrowing.

Arterial Narrowing

The narrowing of arteries in atherosclerosis is a feature which has puzzled observers for the past century. If we accept the long current view that the condition represents a degeneration of the vessel walls, then narrowing seems paradoxical. Arteries are especially constructed to withstand a high internal pressure which is constantly pulsating, and it is their elasticity * which enables them to dilate and recoil again to their original size at each pulse wave, without becoming progressively distended. Any change which weakens them or reduces their elasticity must therefore cause them to give way and dilate rather than become narrowed. Yet in atherosclerosis they are often narrowed almost to the point of occlusion and, as I have reasoned (Duguid 1949), it is difficult to explain this on any other grounds than thrombosis or embolism. When a thrombus forms in an artery it occupies the lumen from the outset and so narrows the blood-stream; and, although in due course it becomes part of the vessel wall, it does so at the expense of the lumen. In this process there is no weakening of the vessel, but merely a reduction of its effective lumen; and, although the thrombus may subsequently shrink, and the lumen become widened again, narrowing must, for a time at least, be the rule.

With the cholesterol lesions it is different, because in them there is no sudden reduction of the lumen but merely a gradual silting up of the walls with foam cells. This must have the effect of reducing their elasticity, and so we find the rabbit's arteries dilated when they are loaded with cholesterol (fig. 4). An exception to this is sometimes provided when small arteries and arterioles become plugged with foam cells, as may happen in the myocardium. In vessels of small calibre a few such cells are often enough to occlude the lumen and bring about a condition equivalent to embolism, but it is usually in very small branches that this occurs and the effects are negligible. When the larger coronary arteries are the seat of cholesterol deposits, dilatation is the rule; and this is one of the most significant points brought out by the experiments. It has always been assumed that fatty changes lead to narrowing of the arteries by increasing the intima so that it encroaches on the lumen, but the cholesterol lesions show that this is not what happens. Thickening of an artery merely impairs its resilience and leads to dilatation. The only process likely to reduce its lumen is one arising in the lumen itself, such as thrombosis or embolism, and we may therefore take it that, where a coronary artery is narrowed by a fibrous thickening of the intima, thrombosis is the most likely factor.

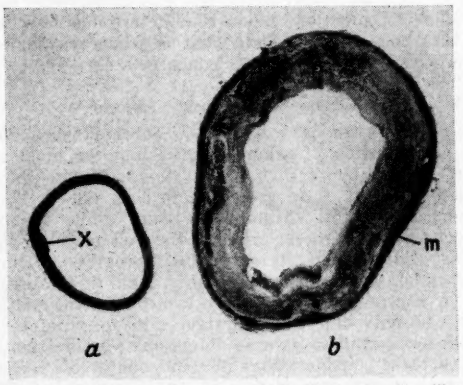

Fig. 4—Ascending aortas from two rabbits illustrating the dilatation which results from cholesterol loading. (Frozen sections: Sudan IV and hæmalum. × 6.)

(*a*) Aorta from rabbit weighing 2800 g. which was on cholesterol treatment for 7 weeks. One small deposit of foam cells is seen at (x) the vessel being otherwise normal. Almost the whole wall consists of medial coat, the intima comprising no more than a single layer of endothelial cells.

(*b*) Aorta from rabbit weighing 2200 g. after $9^1/_2$ months' cholesterol treatment. Most of the wall consists of thickened intima; the media, which is greatly stretched, is represented by the thin dark line (m) at the periphery. (It should be explained that the contrast in diameter is probably somewhat accentuated by post-mortem contraction in the more normal vessel, the thickened vessel being fixed in the position of maximum dilatation by the almost rigid intima.)

* It should be explained that the term elasticity as applied to arteries does not refer to the so-called elastic tissue in their walls but to the resilience of the walls as a whole.

Narrowing as a Feature in Human Atherosclerosis

Thirty years ago pathologists were inclined to look on atherosclerosis—or atheroma as it was then called—as a minor lesion, universal in old age, and only occasionally attended by serious consequences such as cerebral hæmorrhage. In course of time, however, its association with gross myocardial infarction came to be more widely recognised, and today it is regarded as one of the most deadly of lesions, because it leads to narrowing of the coronary arteries with impairment of the cardiac circulation and a tendency to sudden death from thrombosis. Yet these effects are by no means a constant feature of the condition. In old people we often see extreme atherosclerosis with widespread destruction of the arteries but little or no narrowing, and conversely we occasionally find points of extreme narrowing in arteries which are otherwise not very severely affected. There are, in fact, two forms of atherosclerosis—one in which there is narrowing, and which is consequently a highly dangerous condition, and another in which the tendency is rather in the opposite direction.

It would be convenient if we could correlate these two forms with what we have learnt of the pathogenesis, and so infer that all lesions with narrowing were thrombotic, and all others were of a primary fatty nature; but this we cannot do, because thrombotic lesions do not always remain narrowed. Thrombi shrink as they become organised, and arteries which have been narrowed become widened again—sometimes to beyond their original size. Moreover, it is only when thrombi are large in proportion to the vessels they occupy that narrowing is much in evidence. The great majority of mural thrombi consist of no more than microscopic encrustations of fibrin which are too thin to reduce the lumen appreciably. They may if laid down repeatedly on top of one another, give rise to considerable thickenings; but these do not encroach on the lumen to any extent, because such thickenings, by reducing elasticity usually lead to dilatation, and this more than compensates for any encroachment. Thus the arteries of aged people are commonly dilated although many of the lesions in them are obviously thrombotic.

Narrowing is therefore by no means a constant feature of arterial thrombosis; but nevertheless when present it is a fairly sure sign of that process, and, since it is only when there is narrowing that atherosclerosis is likely to be dangerous, it follows that thrombosis is the one factor of importance in fatal coronary disease. When we consider all the possible ways in which thrombosis may be influenced by diet we shall cover a large part of this very involved problem.

Thrombosis and Diet

There are two ways in which diet may conceivably play a part in arterial thrombosis. Firstly it may, by affecting the coagulability of the blood, increase the tendency to clotting; and secondly, by causing fatty changes in the arteries, it may promote mural thrombosis.

The first possibility has recently been suggested by Fullerton, Davie, and Anastasopoulos (1953) who showed that the alimentary lipæmia which follows fatty meals is accompanied by an accelerated clotting-time in vitro. The same was also found by Waldron, Beidelman, and Duncan (1951). As Fullerton and his co-workers point out, a factor of lipid nature is concerned in blood coagulation, and an excessive intake of fat may perhaps increase it. It is well however to recall that there is also a lipid-inhibiting factor in coagulation; and the probabilities may thus cancel out. We do not yet know whether an accelerated clotting-time in vitro actually signifies an increased tendency to thrombosis, and any hypothesis of this kind is difficult to put to the test; but we may justifiably take the evidence of cholesterol experiments, since it is on them that the diet hypothesis mainly rests; and, as it happens, they provide no confirmation. In none of the rabbits were arterial thrombi to be found, in spite of the fact that cholesterol —the substance most frequently cited as the dangerous food constituent—was greatly in excess in the blood. We can only await further information on this point, especially with regard to the phenomenon of coagulation in other species.

The second possibility—that diet may lead to mural thrombosis by damaging the arterial walls—is of course the root of the diet hypothesis. Fatty lesions have long been regarded as the cause of mural thrombosis, and Rannie and I undertook the feeding experiments in the hope that we might demonstrate thrombi in relation to the cholesterol lesions and so bring these into line with coronary disease. But in this we were disappointed. Despite extreme disorganisation of the vessels, there were never any fibrin formations, and we were forced to conclude that neither an excess of cholesterol nor the consequent arterial lesions were in themselves sufficient to promote thrombosis in rabbits.

Nevertheless there can be little doubt that in man arterial lesions play a part in the development of mural thrombosis, for we almost never find such thrombi without some underlying fatty change. Some of the fatty changes are themselves secondary products of thrombi; but others are almost certainly of a primary nature, and, if not dependent on diet, are at least related to some disturbance of the fat metabolism. Superficial fatty streaking of the aorta is probably in this category, and it is not infrequently attended by fine fibrinous encrustations on the aortic surface (Duguid 1948). It can hardly be put down to diet, since it is mostly found in young subjects who have died from acute febrile conditions in which an excessive intake of rich foods is unlikely; but as I have said, lesions of a very similar kind can be seen in older subjects and some of them may be of dietary origin. We know that old people tend to have abnormal lipids circulating in their blood after heavy meals, and they may perhaps get into the arteries and lead to thrombosis. Such is of course the conception on which the diet hypothesis is based, and it is one that cannot be entirely discounted; but it leaves out of consideration one point of paramount importance with regard to vascular thrombosis, and that is its inherent variability.

Factors Governing Arterial Thrombosis

We have seen that the cholesterol lesions do not lead to thrombosis in rabbits, and this is quite in keeping with what we frequently find in man. Few observers can have failed to be impressed with the fact that there may be widespread atherosclerosis of the aorta and other vessels, even with ulceration, and yet little or no thrombosis. We have been given to understand that the rapidity of the blood-stream in the larger arteries limits fibrin formation, and this is perhaps to some extent true; but when on occasion we find quite large mural thrombi in these same vessels, in people who have been active up to the time of death, speed of blood-flow does not seem to be the whole explanation.

To anyone who tries to produce arterial thrombosis in animals by injuring the arteries it becomes evident that there are refractory states, in which thrombi will not readily form, even with severe damage, and irrespective of the speed of the blood-flow. There are also states in which thrombi, having formed, rapidly disappear; and it would seem that there are factors in the blood—possibly anticoagulant substances, or possibly fibrinolysins as suggested by Mole (1948)—which in favourable circumstances control fibrin formation, and so make arterial lesions potentially less dangerous.

On the other hand there are the converse states, which may be described as thrombophilic. In cases of sudden death from coronary thrombosis I have several times noticed that the thrombotic process was not confined to the site of occlusion in the one coronary artery, but was widespread and prominent in the aorta and other vessels. This suggests that, when the fatal occlusion occurred, some thrombogenic influence, more powerful and generalised than mere local damage to the vessel walls, was at work; and this I believe is the factor we must aim at controlling if we are to reduce the incidence of coronary disease.

Undoubtedly intimal lesions are a contributing factor in mural thrombosis; but they are not the controlling factors, for there is no consistent correlation between the severity of the lesions and the size of the thrombi. Sometimes quite large masses of fibrin are formed on lesions which seem comparatively insignificant, and vice versa. It is obviously not the underlying lesion but some factor in the blood that determines how large the thrombus shall be, and that is what counts in so far as vascular impairment is concerned.

The Danger of Fatty Lesions

In the past we have looked on coronary thrombosis as a complication of atherosclerosis, but we must now regard it as a factor in this condition. Where there is much narrowing of an artery there is usually evidence of recurring mural thrombosis; and, while we may suspect that the process arises in the first place on some primary fatty lesion, its subsequent progress is simply a succession of one mural thrombus leading to another. Thus if a primary fatty change comes into the picture, it may be only at the initial stage, and long before the disease has begun to assume dangerous proportions.

With these considerations in mind one is less inclined to attach much importance to the presence of fatty changes. As Geiringer (1950) and others have shown, such changes are an almost constant feature of the aorta from childhood onwards, and we know that they are compatible with long life. They may, it is true, provide the foci in which thrombi develop, when conditions are set for thrombosis; but their severity seems to be a matter of minor importance. Fatal thrombosis is more likely to occur in a coronary artery which is narrowed by a dense fibrous thickening as in (fig. 2) than in one which is very fatty.

The Basis of the Diet Hypothesis

The idea that atherosclerosis is connected with diet arose out of an impression that fatty changes in arteries were prevalent in diabetics, gouty persons, alcoholics, and fat people who had presumably lived well; but we now know that some of the fats which appear in athero-

sclerosis are products of thrombi and are therefore secondary. Since they are probably derived from the lipids present in the blood when the thrombi are formed, it is not surprising that they should be prominent in diabetics and others who are prone to lipæmia. They may in fact be related to diet and yet have nothing to do with the cause of atherosclerosis.

In more recent years the mainstay of the diet hypothesis has been the cholesterol experiments. The fact that arterial lesions can be produced by giving an excess of a normal metabolite seems to put the hypothesis on an unassailable footing until we examine it critically. When we do so we merely find that to produce the lesions far more cholesterol is needed than is ever likely to be derived from a normal human diet, and that when produced these lesions are not of the kind which leads to vascular insufficiency.

The hypothesis therefore rests on slender foundations, and we have, I think, allowed ourselves to be too much influenced by it in our approach to the problem of coronary disease. Certainly much valuable information about the metabolism of fats has been collected, but before we can apply it to coronary disease we must be clear in our minds as to what we mean by that term. If we simply mean fatty changes in the coronary arteries, then we refer to a condition which is almost universal in adults. It may perhaps be related to diet, although there is no clear evidence on that point, but it is not the condition responsible for cardiac impairment and sudden death.

This problem will remain confused until it is more generally recognised that there are two different forms of atherosclerosis involving different pathological processes. They may present similar histological pictures, and they are often indistinguishable, but they are vastly different in their causes and effects. The form with which we are mainly concerned is the one which leads to coronary occlusion, and we know that in this form thrombosis is the important factor. It is possible that diet may have some effect on thrombosis, since nutrition must be a factor in most biological processes; but, when there are so many other important factors to be considered, there is a danger in allowing ourselves to be led too far along this line of approach by what may be a misleading hypothesis.

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"I should like to suggest that intelligent behaviour may admit of differences in kind as well as in degree. For me, intelligent activity consists in grasping the essentials in a given situation and responding appropriately to them. This can scarcely claim to be a definition and it is certainly not precise. I prefer 'intelligent activity' to 'intelligence' because I wish to avoid the suggestion of some one trait which an individual simply possesses, to a greater or lesser extent. I use the word 'activity' in its widest sense, not necessarily implying activity which is overt at the time."—A. W. HEIM, *The Appraisal of Intelligence*, London, 1954, p. 29.

AUGMENTED RESPIRATION

AN EMERGENCY POSITIVE-PRESSURE PATIENT-CYCLED RESPIRATOR

IAN DONALD

M.B.E., M.D. Lond., B.A. Cape Town, M.R.C.O.G.

READER, INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY, UNIVERSITY OF LONDON

THE principle of augmented respiration—in which spontaneous respiratory effort is amplified—has already been discussed, and the servo respirator used for the purpose has been described (Donald and Lord 1953). Experience has shown, however, that in treating respiratory difficulties in the newborn there is also need for an emergency type of apparatus which can be brought into action more rapidly. The servo respirator is not always readily available, and the staff who can handle it have to be mustered. Moreover, in spite of our efforts to forecast the likely course of events, with the help of radiography (Donald and Steiner 1953) and spirometry, delays often arise from the difficulty of deciding whether the baby really needs to be put in the servo respirator. When signs of respiratory distress develop—usually soon after delivery—it is far from easy to say whether spontaneous recovery is likely to take place; and in some cases a series of cyanotic attacks may be the first warning of trouble.

Of the 28 infants so far treated with the servo respirator, those whose treatment began before the age of three hours have done much better than those treated later.

In table I asphyxial deaths include cases of atelectasis (with and without hyaline membrane formation), and cases of intraventricular hæmorrhage, which is nearly always the result of asphyxia (Claireaux 1953b), and then operates as a secondary cause of further asphyxia. In 7 cases the infants were non-viable, being of less than twenty-eight weeks' gestation; and, since there was no question of their maintaining respiration, treatment was started without delay. Hence they all appear in the group in which treatment was started before the age of three hours. In this group 1 viable child died of hyaline membrane, and in this instance the respirator had failed mechanically.

To cover delays in preparing the servo respirator or to meet respiratory emergencies we clearly needed a respirator which could be operated at once via a mask, with the child still in its cot or incubator.

Our routine treatment of a cyanotic attack consists in pharyngeal, œsophageal, and gastric aspiration, with administration of gastric oxygen; but, if the child does not quickly revive, a respirator is used. Intubation of premature or very sick neonates is not well tolerated, and, without intubation, positive pressures applied to the face without regard to the timing of the child's respiratory efforts tend simply to drive air or oxygen down the œsophagus into the stomach. If on the other hand, a positive pressure is applied synchronously with contraction of the diaphragm in inspiration, it closes the

TABLE I—RESULTS WITH SERVO RESPIRATOR (28 CASES)

	Age under 3 hours 10 + (7) cases			Age over 3 hours 11 cases		
Weight (lb.)	Lived	Died from asphyxia	Died from other causes	Lived	Died from asphyxia	Died from other causes
−2	0	(2)	(4)	1	0	0
2–3	4	1+(1)	0	1	1	1
3–4	4	0	0	1	2	1
4–5	1	0	0	0	1	1
5+	0	0	0	0	1	0
Total	9	1+(3)	(4)	3	5	3

Figures in parentheses indicate previable fœtuses of less than 28 weeks' gestation.

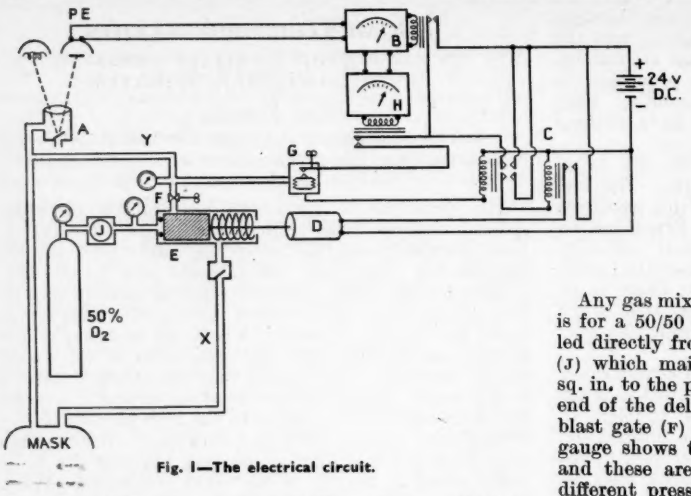


Fig. 1—The electrical circuit.

lower end of the œsophagus and allows the gases to take their intended route to the lungs—which alone are likely to achieve rapid oxygenation of the blood. The principle of augmented respiration therefore applies.

The Apparatus

For short-term emergency treatment we now use a positive-pressure patient-cycled respirator—known locally as "the puffer."

As in the servo respirator, the triggering of intermittent pressures is achieved by a photo-electric mechanism, in which the flap of the inspiratory valve consists of a mirror (A) (figs. 1 and 2) whose slightest movement deflects a light-beam from a photo-electric cell (P.E.). The beginning of an inspiratory effort thus causes a change in voltage output from the cell. This is amplified (B) to operate the electromagnetic relay system (C) which controls the solenoid (D). The solenoid moves the piston valve (E), which not only closes off the exhaust pipe (X) from the face-mask but opens the delivery pipe (Y) through which a suitable gas mixture is fed under direct pressure to the face-mask. A blast gate (F) adjusts the rate of flow of gas. By means of an aneroid switch (G), which interrupts the circuit, pressures are prevented from exceeding a pre-set maximum.

The amplifier (B) includes the refinement of a "paralysis time" circuit which introduces a refractory phase and allows the amplifier to pass on only the first impulse from the photo-electric cell and to reject all others over a pre-set period—usually about a second. This prevents false and repetitive triggering.

A "hold-in" time circuit (H), in this case an 'Elcontrol Weld Timer' switch, is also necessary to keep the solenoid in action for a predetermined period after each triggering—in case sufficient pressure is not built up to operate the aneroid switch (G). H and G are connected in series so that the circuit shall be interrupted by the aneroid pressure cut-out switch or by the hold-in timer, whichever operates first. In other words, if the maximum permitted pressure is achieved before the hold-in time has expired, the solenoid will be inactivated, the spring behind the piston valve will shut off the supply of compressed gas mixture, and the expiratory pipe will be opened; but if (perhaps because the mask does not fit) the pre-set pressures are not achieved within the hold-in period, the time switch will first interrupt the supply of gas. This prevents the solenoid from holding the piston valve in the open position which would otherwise continue indefinitely and waste the gas mixture.

The hold-in time and the paralysis time must not be allowed to overlap, and the former must be adjusted not to equal or exceed the latter.

Thus at the completion of each cycle, the apparatus is ready to respond to the next triggering from the inspiratory valve.

Any gas mixture can be supplied. Our usual preference is for a 50/50 mixture of oxygen and nitrogen, which is led directly from a cylinder to a pressure-reducing valve (J) which maintains a delivery pressure of 1·8 lb. per sq. in. to the piston valve. The pressure at the proximal end of the delivery pipe to the mask is adjusted by the blast gate (F) to about 30 cm. of water. A manometer gauge shows the pressures achieved in the mask itself, and these are usually about 15 cm. of water, though different pressures can be achieved at will. The mask is simply a soft rubber U.S. Army resuscitation mask applied *upside down* so that the baby's chin fits into the apex which would normally lie over the bridge of an adult's nose. The base of the mask lies over the baby's forehead, and with a very little practice almost any size or shape of face can be satisfactorily fitted. The mask can be lightly held in place by spreading the fingers round the sides.

The aneroid switch controlling the maximum permitted pressure, and the "hold-in" and "paralysis" times seldom require adjustment, and all that is necessary in a given emergency is to switch on the apparatus, turn on the gas supply, and (having aspirated the pharynx) apply the mask to the face—the whole operation taking no more than a minute.

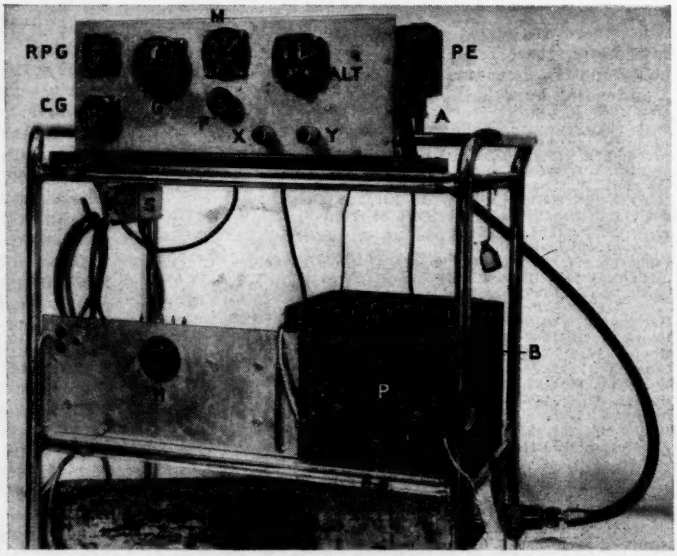
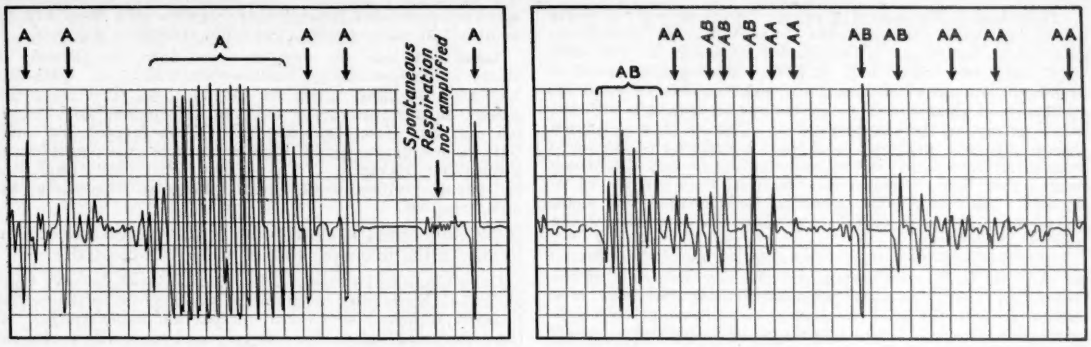


Fig. 2—Photograph of the puffer respirator.

A. Inspiratory mirror flap valve.
P.E. Photo-electric cell box.
B. Amplifier.
ALT. Altimeter barometer.
X. Exhaust pipe } to mask.
Y. Delivery pipe }
F. Blast gate.
G. Aneroid cut-out switch.
P. Paralysis-time controls.
H. Hold-in time control.
M. Manometer (cm. H_2O X 10).
C.G. Cylinder gauge.
R.P.G. Reduced-pressure gauge.
S. Switchbox.



(a) (b)

Fig. 3 (case U.C.)—Tracings obtained with Smyth anenometer. (a) Spontaneous respiration amplified at A with puffer. (b) AA = non-triggered amplification. AB = patient-triggered amplification.

If the baby has stopped breathing altogether, and for the moment there is no respiration to amplify, an occasional pinch and release of the delivery tube (Y) is sufficient to trigger off a surge of positive pressure to the mask. This has none of the advantages of augmenting respiration; but when the baby does take a breath, even though small, that breath will instantly be increased.

Fig. 3 shows that much greater ventilation is achieved when spontaneous respiration is amplified than when gases are supplied under pressure without regard to the child's own respiratory efforts. This tracing was made at University College Hospital by Dr. Norman Smyth who applied his nasal anemometer apparatus underneath my mask. It gives an indication of the rate of flow of gas through the nostrils.

Application in the Adult *

Although the apparatus was originally intended for babies, my colleagues in the department of medicine of the Postgraduate Medical School, Dr. Russell Fraser and Dr. Charles Fletcher, encouraged me to adapt it for adult use. This was done quite simply by fitting alternative large-bore delivery pipes. It was not long before an opportunity arose for treating an adult, and I am indebted to Prof. Ian Aird for permission to describe the following case.

The patient, a woman aged 62, had a straightforward cholecystectomy. A curare derivative was used to obtain relaxation, and after the operation, which lasted just over an hour, spontaneous respiration did not return, despite intravenous injection of nikethamide, atropine, and neostigmine. For more than five hours artificial respiration was continued by rhythmic squeezing of the bag of the anæsthetic machine, and during this time a total of 8·5 mg. neostigmine methyl sulphate and atropine gr. $^1/_{12}$ was given. After three and a half hours feeble spontaneous respiration began, but it was inadequate without continued assistance and a cabinet respirator was sent for.

About five and a half hours after the operation, while the arrival of the cabinet respirator was awaited, the puffer was applied, the patient's spontaneous respiratory efforts being sufficient to operate the sensitive trigger mechanism. Her colour at this time was somewhat grey. After five minutes' treatment with the apparatus an adequate depth of respiration was achieved, and this was maintained thereafter spontaneously. The corneal reflex returned and half an hour later she was returned to the ward showing signs of regaining consciousness. The systolic blood-pressure now dropped precipitately to 60 mm. Hg, but her general condition responded to routine resuscitative measures. Convalescence was complicated by a small pulmonary embolus after the first postoperative week, but was then straightforward.

In this case the use of the apparatus was immediately followed by return of adequate spontaneous respiration. The patient was not intubated at the time, and if, as I think probable, she was suffering from prolonged pulmonary underventilation, with accumulation of carbon dioxide, her recovery may well have been due to removal of this carbon dioxide with the help of the apparatus.

Results in the Treatment of Neonates

Up to the end of 1953, 25 cases had been treated with the puffer. Of these, 4 were also (and mainly) treated with the servo respirator and therefore appear in table I. The remaining 21 cases are analysed in table II.

It is our practice to keep the puffer standing by, adjusted and ready for immediate action in cases of severe prematurity or where attacks of respiratory failure threaten. Certain members of the nursing staff in the Premature Baby Unit at Hammersmith Hospital are now capable of handling the apparatus well and have repeatedly been able to restore satisfactory respiration and oxygenation before medical help arrived.

It must here be repeated that the apparatus is not used without first thoroughly aspirating mucus from the pharynx.

NON-SURVIVING CASES

Intraventricular hæmorrhage was the predominant cause of death in 4 of the 14 non-surviving cases and hyaline membrane was also present in 2 of them. One had a tear of the tentorium. Except in one of the cases demonstrating hyaline membrane in marked degree, all lobes of the lungs floated at necropsy. In 3 of the above cases the period of gestation was less than twenty-eight weeks and the infant was therefore not viable.

Atelectasis with hyaline membrane was responsible for death in a further 5 cases, in 2 of which intraventricular hæmorrhage was also a contributory factor. In a 6th case hyaline membrane was present but the primary cause of death was intrapulmonary hæmorrhage.

The following case is worth quoting because a mild degree of pulmonary damage was sustained.

TABLE II—RESULTS WITH PUFFER ALONE (21 CASES)

Weight (lb.)	Lived	Hyaline membrane	Intraventricular hæmorrhage	Hyaline membrane and intraventricular hæmorrhage	"Asphyxia" unspecified	Intrapulmonary hæmorrhage
−2	0	0	(1)	(1)	0	0
2–3	3	1	0	(1)	0	1
3–4	1	1	1	1	1	0
4–5	2	1	0	1	0	1
5+	3	0	0	0	0	0
Total	9	3	1+(1)	2+(2)	1	2

Figures in parentheses indicate previable fœtuses of less than 28 weeks' gestation.

* A fair copy of my prototype apparatus is now being developed by British Oxygen Company Ltd.

Case Lo2.—The second of twins; breech delivery at thirty weeks' gestation; birth-weight 2 lb. 10 oz. At birth lively and pink, but signs of inspiratory recession of the chest wall developed within half an hour. Radiographs taken at one hour, six and a half hours, and eighteen hours showed the evolution of signs which we have come to associate with the development of hyaline membrane. The child was treated repeatedly with the puffer and then transferred to the servo respirator from which it was removed at the age of thirteen and a half hours because its condition then seemed satisfactory. One hour later, however, its condition was again very poor. It was repeatedly aspirated, and revived with the puffer.

After replacement in the servo respirator, the child appeared to progress fairly well throughout the day until one of the valves in the apparatus jammed. The puffer was now connected with the head chamber in order to supply positive-pressure assistance. Meanwhile the faulty valve was repaired.

All went well thereafter until the age of twenty-four hours when a series of cyanotic attacks recurred. At twenty-five hours the child was again breathing very well without augmentation. During the next four hours the colour gradually deteriorated but the respirator was not switched on again because the breathing appeared to be fairly regular. At twenty-nine and a half hours the child died in a prolonged apnœic attack which both machines operating simultaneously failed to modify.

At necropsy there was severe emphysema of the left lung. Four large bullæ were present in the posterior medial margin of the left upper lobe and there were numerous smaller emphysematous bullæ throughout this lobe. The use of servo respirator and puffer simultaneously may have been responsible for the emphysema. Dr. Claireaux, who performed the necropsy, did not regard the emphysema as the cause of death and he reported extensive hyaline membrane. There was no pneumonia.

There were 3 cases in which the cause of death could not be definitely determined other than as "asphyxia." One of these infants weighed only 1 lb. 6$^3/_4$ oz. and, having been treated in the servo respirator as well, is included in table I. Pulmonary æration was no more than moderate in all of them, but all lobes of the lungs floated at necropsy. The usual picture histologically was that of areas of atelectasis alternating with areas of over-distension.

SURVIVING CASES

Of the 11 infants who survived, 2 were also treated in the servo respirator and therefore appear in table I instead of in table II. The largest weighed 5 lb. 8$^1/_2$ oz. and the smallest 2 lb. 6 oz. The indications for treatment were the appearance of severe and increasing inspiratory recession of the thoracic wall, the development of apnœic and cyanotic attacks, or very shallow and infrequent breathing associated with clinical signs of cyanosis. As these babies survived it is impossible to discuss the underlying pathology treated.

Case Na, weighing 2 lb. 6 oz., was delivered in a nursing-home at thirty weeks' gestation and was admitted aged eighty minutes. The condition deteriorated at three and a half hours and multiple cyanotic attacks necessitated the use of the puffer intermittently at each attack during the first three days of life. Radiographs showed fine miliary stippling of the lungs which became more conspicuous and coarser by ten hours but cleared by sixty hours. At the age of twenty-three days the child developed pneumonia but recovered and has since done well.

Case Va was delivered spontaneously face to pubis at thirty-nine weeks' gestation and weighed 4 lb. 15 oz. The condition at birth was one of shock and the child was intubated. Positive pressures were applied endotracheally by the usual routine method for sixty minutes without spontaneous respiration becoming established. The puffer was then used and the child quickly recovered and did well thereafter. Possibly a very lucky coincidence.

Case Oa.—Breech delivery at thirty-two weeks; birth-weight 3 lb. 5 oz. Inspiratory recession and grunting respiration were soon apparent. The puffer was used repeatedly during the first six hours of life, during which time trip spirometry showed considerable improvement from 420 ml. to over 700 ml. per min. The child thereafter did well.

Case Lo1 was the first of twins born precipitately at thirty weeks' gestation. Birth-weight 2 lb. 7 oz. Pethidine had recently been given to the mother. The child was apnœic and obviously narcotised, and nalorphine ('Lethidrone') 0·5 mg. was given into the cord. This revived the child, but its colour remained blue and there was considerable inspiratory recession. The puffer was then used and its colour improved at once. Progress thereafter was uninterrupted.

Nalorphine greatly contributed to the successful outcome here. In the following case it was given belatedly.

Case Go.—Birth-weight 2 lb. 12 oz. Rapid delivery three and a half hours after morphine had been given to the mother because of mixed accidental antepartum hæmorrhage. At birth the child was flaccid and grey and took only occasional gasps. Gastric oxygen had no apparent effect. The puffer was thereupon used—without much immediate benefit, for the respirations were infrequent. Nikethamide 0·25 ml. was injected intravenously, with transient benefit, and treatment with the puffer was continued. At sixty minutes nalorphine (0·5 mg.) was injected, and regular but slow respiration was established at once. Treatment with the puffer was continued for another half-hour but the colour did not become really satisfactory until a high oxygen concentration was given by the apparatus.

In this case the Coombs test was strongly positive, and after a replacement transfusion the child did well. The nalorphine should have been given earlier.

Case Ee.—Normal delivery at thirty-seven weeks' gestation. Birth-weight 5 lb. 2 oz. This child did not appear to be breathing satisfactorily and at one hour fifty minutes the minute volume was only 330 ml. Fifteen minutes' continuous treatment was given with the puffer at the age of two and three-quarters hours. I was not present personally but my colleagues noted improvement clinically, and at four hours thirty-five minutes the minute volume was 550 ml. Progress thereafter was uneventful.

Case Bo.—Spontaneous premature delivery at thirty-one and a half weeks following premature rupture of the membranes for the preceding two and a half weeks. Birth-weight 4 lb. 2$^1/_2$ oz. The child cried at birth but severe recession developed within four minutes. The colour was poor and treatment with the puffer was given intermittently with benefit. The signs of inspiratory recession gradually disappeared within a few hours.

The apparatus was here used intermittently to correct evident asphyxia. It is unlikely that it directly influenced the disappearance of the recession.

Case U.C.—Rapid delivery at term with fœtal distress in the second stage. Birth-weight 5 lb. 8$^1/_2$ oz. The child refused to take more than occasional gasps and its colour remained very poor.

Delivery had taken place at another hospital and I was asked to see the case because there were no signs of spontaneous improvement during three hours. I took the puffer with me, and treatment was started at approximately the age of four hours and maintained by my enthusiastic colleagues at this hospital for nearly three hours in spite of my gloomy forecasts. It seemed certain that the child had an intracranial hæmorrhage and I doubted whether it was worth persisting. Dr. Norman Smyth, however, applied his anemometer under the face-mask, and fig. 3 is a sample of the tracings obtained. Ventilation appears to have been increased. The child slowly recovered and is now eleven months old and progressing normally.

Case Ar.—District delivery at approximately thirty-four weeks. Birth-weight 3 lb. It cried well at birth. On admission at three hours, the temperature was 95°F. Cyanotic attacks repeatedly occurred and intracranial bleeding was provisionally diagnosed. Nevertheless the puffer was used repeatedly to restore oxygenation and after the age of twenty-four hours no further cyanotic attacks occurred. Apart from subsequent difficulty with feeding the child has since done well.

The salvage of babies suffering from intracranial bleeding might be regarded by some as questionable;

but, since the diagnosis cannot be made with certainty before death, it is worth giving the child the benefit of the doubt, as these last two cases indicate.

Summary and Conclusions

Further experiences in augmented respiration showed the need for an emergency type of respirator as an ancillary to the main servo respirator.

A positive-pressure patient-cycled respirator, operated via a face-mask, is described and the results of its use are briefly reported.

The recovery of the surviving infants cannot necessarily be attributed wholly to the use of the respirator; but our observations have at least shown that, at the pressures normally employed, the treatment is harmless and temporarily beneficial. Its object is no more than to combat asphyxia for the time being and so allow the child time in which to achieve normal respiration if it is capable of doing so.

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HYPOCHROMIC ANÆMIA IN R.A.F. RECRUITS

B. J. LEONARD
M.D. Manc.
SQUADRON-LEADER, R.A.F.
From the Royal Air Force Hospital, West Kirby, Cheshire

IDIOPATHIC hypochromic anæmia in the male has been regarded as rare.

Wintrobe (1951) suggested that, if hypochromic anæmia was found in a man it was almost always caused by occult loss of blood, unless there had been a gastric operation.

Whitby and Britton (1950) describe the condition as exceedingly rare in males. Faber (1913), who first drew attention to this disease, reported 3 cases in males out of 20 cases; Davies (1931a) 4 cases in males out of 55 cases, and Witts (1930) 1 case; and Britton (1936) found 4 cases in males out of 66 cases.

Witts and Burgher (1934) published 26 cases in males, of whom 8 were aged less than thirty; they noted a tendency to immaturity in the lower age-group. Filo (1933) described eunuchoidism or underdevelopment of the genitalia with this type of anæmia in young males. Thomson (1943) found 9 cases of hypochromic anæmia in adolescent males, of whom 4 had splenomegaly.

Shorthouse and King (1951), who described 20 cases of hypochromic anæmia in army recruits, also discovered a tendency to immaturity and noted that the symptoms did not appear until after a few months' service.

This paper deals with 50 cases of hypochromic anæmia detected by routine blood examination of young men on entry into the Royal Air Force, which have been investigated and treated at this hospital. As all these men had recently undergone medical examinations to assess their fitness for military service and had all been passed grade 1, there is evidently some clinical difficulty in detecting the condition. The investigations were designed to attempt to answer the following questions:

(1) What is the incidence of anæmia in R.A.F. recruits?
(2) What types of anæmia are we dealing with?
(3) What are the social background, symptoms, and clinical signs of anæmia in the young male?
(4) How should these cases be treated?

Methods

Hæmoglobin values (oxyhæmoglobin method) were estimated in 1000 recruits in their first week of training. After this all of 3221 recruits entering the camp were screened by the copper-sulphate method. The total number of recruits examined was therefore 4221. Among these, 50 were found to be undoubtedly anæmic (Hb 12 g. or less per 100 ml.) and were admitted to a special ward for investigation and treatment.

The following determinations were made on 5 ml. of venous blood: (1) hæmoglobin (Medical Research Council grey-wedge photometer); (2) packed-cell volume; (3) red-cell count; (4) absolute values; (5) total and differential white-cell count; (6) reticulocyte-count; (7) erythrocyte-sedimentation rate (E.S.R.); and (8) blood fragility.

The following tests were also done as a routine: (1) fractional test-meal (combined alcohol and histamine method); (2) benzidine test (occult blood was tested for on three consecutive daily samples of fæces); (3) a mid-stream specimen of urine was examined for albumin, sugar, and deposit; (4) radiography of the chest; (5) total fæcal fat (in many cases a four-day fat-balance test was made); and (6) examination of bone-marrow.

In the presence of gastric hyperacidity and a history suggesting peptic ulceration, or, if occult bleeding was detected, the whole of the gastro-intestinal tract was radiographed.

Findings

Of these 50 men with hypochromic anæmia 2 had bleeding from the gastro-intestinal tract and 1 acholuric jaundice. In the remaining 47 no cause of the anæmia was detected, and the condition must be regarded as idiopathic (table I).

TABLE I—BLOOD FINDINGS

Case no.	Hb (g. per 100 ml.)	Hb* (%)	Packed-cell vol. (%) (normal average 47)	Red cells (million per c.mm.)	M.C.H.C. (%) (normal average 33)	Mean corpuscular volume (c.μ) (normal average 90)	White cells (per c.mm.)
1	4·9	33	28	3·8	18	74	8400
2	6·6	44	31	3·9	21	79	8400
3	6·9	46	31	4·0	22	78	5300
4	7·3	49	33	5·1	22	65	3000
5	7·4	49	33	4·2	22	79	9400
6	7·5	50	34	4·5	21	76	7400
7	7·6	51	33	5·2	23	63	7000
8	7·6	51	37	4·1	21	90	5100
9	7·6	51	34	4·3	22	79	3600
10	7·7	52	36	4·8	21	75	5200
11	8·0	54	34	4·9	23	69	7500
12	8·0	54	36	5·0	22	72	6000
13	8·0	54	35	5·3	23	66	5700
14	8·2	55	31	4·5	26	69	6600
15	8·3	56	33	4·4	25	75	5000
16	8·3	57	34	5·2	25	60	5400
17	8·5	57	34	4·7	25	72	4500
18	8·8	59	36	4·6	24	78	7600
19	9·0	60	35	4·7	26	74	3400
20	9·0	60	34	4·9	26	76	4800
21	9·0	60	38	4·8	23	79	5100
22	9·3	62	37	4·7	25	79	8300
23	9·6	64	35	4·7	27	74	4300
24	9·6	64	35	5·1	27	69	5300
25	9·8	66	39	3·7	25	105	5400
26	9·8	66	42	4·9	23	86	6000
27	9·9	66	40	4·9	25	82	5000
28	10·0	67	38	4·4	26	87	7000
29	10·0	67	43	5·2	24	83	8300
30	10·0	67	40	5·3	25	73	7300
31	10·1	68	40	4·8	25	83	6800
32	10·1	68	38	5·0	27	76	7000
33	10·3	69	40	4·1	25	97	5800
34	10·3	69	39	4·9	26	80	8600
35	10·3	69	38	4·8	27	79	5100
36	10·3	69	41	4·2	25	97	6000
37	10·4	70	39	4·9	27	80	3300
38	10·6	71	37	4·2	29	88	6500
39	10·6	71	35	4·8	30	73	12,300
40	10·6	71	40	5·0	25	80	10,300
41	10·7	72	39	4·9	26	80	8200
42	10·8	73	41	4·8	26	85	5600
43	11·0	74	43	5·2	26	83	7100
44	11·0	74	39	4·9	28	79	6000
45	11·7	78	38	4·8	31	79	5800
46	11·7	78	39	5·1	30	77	6400
47	12·0	80	43	4·9	28	78	6400

* 100% = 14.8 g. per 100 ml.

THE PATIENTS

Incidence.—In 36 (0·9%) of 4221 R.A.F. recruits aged from eighteen to twenty the hæmoglobin was less than 10·4 g. per 100 ml., and in the remaining 11 (0·2%) it was 10·4–12·0 g. per 100 ml. (table I).

Social Background.—The occupations of the recruits before enlistment did not appear to be significant, but this might well be expected in youths aged eighteen. The social classification of their fathers is a more reliable indication of their background:

Fathers' occupations	*No. of patients*
Unskilled	24
Semi-skilled	8
Skilled	2
Unemployed	7
Fathers dead	6

It can be seen that in most cases the fathers followed unskilled occupations and would come under social class IV or V of the Registrar-General's classification of the population. The number of fathers who, through either ill health or death, were not wage-earners, was high—13 out of 47.

Size of Family Unit.—The average number of siblings for each patient was three.

Geographical Distribution.—Most of the patients came from the North and Midlands, but the significance of this cannot be assessed without figures for the whole of the R.A.F.

SYMPTOMS AND SIGNS

Most of the patients had no symptoms at all, and only 1 had visited his family doctor because of symptoms caused by anæmia. 9 (19%) complained of breathlessness and tiredness of a very mild degree. Dyspepsia and diarrhœa were not complained of, even by those with achlorhydria. A family history of anæmia was reported by 2 patients, but without examining the blood of their parents and relatives this figure might be very misleading.

Their appetites were very good—a fact verified on the ward at mealtimes. Only 4 disliked meat and green vegetables or other iron-containing foods.

The unreliability of pallor of the skin as a sign of anæmia was confirmed, 34 out of 47 having no such pallor. Pallor of the conjunctivæ, gums, and nail beds were almost constant features. Flattening of the nails was seen in 11 (23%), but only 1 had definite koilonychia. The spleen was palpably enlarged in 2 but became impalpable after treatment. Most of the patients appeared dull and lifeless, and their facial expressions depicted easy fatigability. They were of all heights from 5 ft. 2 in. to 6 ft. 5 in. and most of them were built proportionately to their height; none showed signs of loss of weight. As a group they did not show immaturity or underdevelopment of the genitalia.

The 1 man (case 2, with Hb 6·6 g. per 100 ml.) who had significant symptoms before enlistment was a farm labourer aged eighteen and 6 ft. 3 in. tall who had been dismissed by his employer for not pulling his weight. On two occasions he had had severe dyspnœa while doing farm work. Treatment with an iron tonic had improved the dyspnœa on both occasions. Each attack of dyspnœa coincided with the threshing season, when an extra physical effort was required of him; during the rest of the year he had carried on with his farm work without symptoms. This case demonstrates how symptoms due to anæmia must be assessed according to physical effort required by the patient's occupation and other activities.

BLOOD FINDINGS

The low mean corpuscular hæmoglobin concentration (M.C.H.C.) confirmed a state of iron deficiency, and some recruits were severely anæmic (table I). Wintrobe (1951) regards a M.C.H.C. of 22% or less as indicating extremely severe anæmia. In 10 patients the M.C.H.C. was 22% or less. Microcytosis was not found to be a prominent feature, and the red-cell count was normal in most cases. Microcytosis and a low red-cell count may well be features of a long-standing case.

The appearance of the red cells invariably showed variation in staining, shape, and size. The more severe the anæmia the more pronounced were these findings and the greater was the percentage of cells affected. Elliptical red cells, seen in several films, disappeared after treatment and thus excluded elliptocytosis. Scanty stippling of the red cells was seen in a few blood films, but nucleated red cells were not seen. The presence of target cells and moderate anisocytosis with hypochromic anæmia seems to be a good indication to look for steatorrhœa (Cooke et al. 1948); several such cases have been seen in this laboratory.

The total white-cell count was normal, and there was no considerable granulocytopenia. The reticulocyte-count in most of the cases was significantly less than 1%, and in none did it exceed this figure. The platelets appeared normal in number, shape, and size. The E.S.R. and red-cell fragility were always normal.

BONE-MARROW FINDINGS

No published work on the marrow picture in this type of anæmia in young males could be found. Bone-marrow examinations were made in 37 patients. The method of taking the marrow, the staining, assessment, and terminology were those described by Israëls (1948).

The marrow was hyperplastic in 31 and normal in the remaining 6. Usually the lower the hæmoglobin, the more hyperplastic was the marrow. The hyperplasia involved all forms of the normoblastic series. The normoblasts were smaller than normal and the cytoplasm reduced in quantity and basophilic in tint. Table II shows that the range found for the various types of normoblasts included a higher upper limit in all forms.

Hæmocytoblasts did not share in the hyperplasia in any marrow examined. In many films the increase was mainly in the pro-erythroblasts and early basophilic normoblasts. Megaloblasts were not seen in any film. The nuclei of many of the early basophilic erythroblasts were not absolutely typical of any stage in the normoblast series, but a megaloblastic nuclear pattern was certainly not present. Whether these cells could be classified as transitional megaloblasts is open to question (Innes 1949, Israëls 1951). Giant metamyelocytes were not seen in any film, and primitive white cells were not found to be increased in number.

In the hæmoglobin range of 4·9–9·0 g. per 100 ml. the average myeloid/erythroid ratio was 1·9/1·0. In the higher hæmoglobin range of 9·1–10·8 g. per 100 ml. the average ratio was 2·5/1·0. Usually the lower the hæmoglobin, the more closely the myeloid/erythroid ratio approached unity. A ratio of 1/1 or less was never found, even in the severest anæmia.

The bone-marrow findings concur with Leitner's (1949) statement that only a moderate degree of normoblastic hyperplasia is usually found in iron-deficiency anæmia. Whitby and Britton's (1950) statement that normoblasts of various grades of maturity form 50% or more of the total nucleated-cell count was not confirmed in any case in this series.

TABLE II—NORMOBLAST SERIES

Forms	Normal range (%) (Israëls 1948)	Range found (%)	Average (%)
Pro-erythroblasts	0·5–4·0	0·5–5·0	2·6
Early normoblasts	1·0–5·0	2·0–11·0	5·6
Intermediate normoblasts	12·0–20·0	4·0–25·0	15·4
Late normoblasts	6·0–10·0	4·0–12·0	7·0

TABLE III—RESULTS OF TEST-MEALS

—	Achlorhydria (%)	Histamine-fast achlorhydria (%)	Normal acidity (%)	Hypochlorhydria (%)	Hyperchlorhydria (%)
Davidson and Fullerton's (1938) series in females ..	64·9	45·6	17·5	14·6	3·0
Present series ..	62	43	25		13

RELATION OF GASTRIC ACID TO ANÆMIA

Bennett and Ryle (1921), using the gruel test-meal, discovered 4 cases of achlorhydria (not histamine-fast) in 100 healthy medical students.

Lander and Maclagan (1934) found an incidence of 1% after the injection of histamine in a comparable series. Doig et al. (1950) found 1 case of histamine-fast achlorhydria in 134 students.

Fractional test-meals were given as a routine in the present series. 50 ml. of 7% alcohol was given, and 0·5 mg. of histamine was given if no free hydrochloric acid was found.

Table III shows the fractional test-meal findings in this series compared with Davidson and Fullerton's (1938) findings in middle-aged women, with idiopathic hypochromic anæmia. The incidence of achlorhydria and histamine-fast achlorhydria in the two series are virtually the same. In the present series hypochlorhydria was not separated from normal acidity; the dividing line is arbitrary, and the level of acid depends to some extent on whether alcohol or gruel is used. Davidson and Fullerton (1938) emphasised the importance of diet in the ætiology of achlorhydria.

In this series almost every patient had a good appetite, and most of them were taking a reasonable amount of meat, vegetables, and fruit. The findings of comparable incidences of achlorhydria in young men and middle-aged women suggests that the achlorhydria precedes the anæmia or else comes on early in the development of idiopathic hypochromic anæmia.

Davidson and Fullerton (1938) suggested that histamine-fast achlorhydria might not necessarily be permanent. Fractional test-meals were repeated in 13 of the present cases with histamine-fast achlorhydria, from six to ten weeks after the start of treatment, when the hæmoglobin had returned to normal. 6 cases showed free hydrochloric acid—3 without histamine and 3 only after the injection of histamine. These findings are contrary to the generally accepted view on the irreversible nature of histamine-fast achlorhydria, and are hard to explain on any other ground than that of improvement in the blood hæmoglobin, with consequent increase in oxygenation of the gastric mucosa.

Achlorhydria was present in 16 of 21 patients with Hb 9 g. or less per 100 ml., and in 13 of 26 patients with Hb more than 9·1 g. per 100 ml. Although the series is small, this suggests a relation between achlorhydria and the hæmoglobin level. Davies (1931b) studied the gastric contents in cases of anæmia with achlorhydria and found that gradually progressive stages of secretory failure may occur, and that a link between idiopathic hypochromic anæmia and pernicious anæmia, on the basis of failure in gastric secretion, might be postulated.

It is interesting to postulate that there may be two types of histamine-fast achlorhydria, which could be differentiated by histological examination of the gastric mucosa:

(1) *Congenital* (and perhaps familial).—The acid secretory cells either may not have developed in the fœtus, or may be hypoplastic and unable to produce acid. If this type is associated with iron-deficiency anæmia, treatment would not restore the secretion of acid.

(2) *Acquired.*—Some pathological process or processes may cause the oxyntic cells of the stomach to stop producing acid. The histological picture in the early stage might be quite different—i.e., no lack of development of the oxyntic cells. In this type early detection and efficient treatment may restore the secretion of acid. If, however, the anæmia is long-standing, as in typical idiopathic hypochromic anæmia of women, the prolonged anoxæmia might permanently damage the gastric mucosa, and treatment would not alleviate the histamine-fast achlorhydria.

Treatment

The cases reviewed here were all treated with intravenous iron ('Neo-ferrum,' Crookes) because oral iron therapy was slow and unreliable. Saccharated oxide of iron was given in a dosage of 50 mg. on the first day, 100 mg. on the second day, and 200 mg. daily thereafter until the total dosage prescribed had been given. The total dosage was calculated as 25 mg. for every 1% deficit of Hb, the aim being to increase the Hb to 15 g. per 100 ml. No extra iron was allowed for depleted stores. Slack and Wilkinson (1949) showed that, in chronic infections, more than 25 mg. per 1% deficit of hæmoglobin was required, and a full response to this amount therefore helps to rule out chronic infections. Similarly, in idiopathic steatorrhœa and anæmias due to vitamin deficiencies, 100% utilisation of the iron administered would not be expected, because many patients would require folic acid, or the vitamin in which they were deficient, to restore the blood picture to normal.

The average daily increase in hæmoglobin was 0·34 g. at ten days and 0·19 g. at four weeks. The utilisation of the preparation was 100%. In most cases a small reticulocyte peak developed between the sixth and the eighth days but never exceeded 4%. The height of the peak had no constant relationship to the initial hæmoglobin level or the initial red-cell count. A reticulocyte-count of 2–3% after it had been less than 1% for several days was taken to be a definite reticulocyte response. A temporary erythrocytosis (packed-cell volume more than 50%) was noted in nearly every case and accounted for the M.C.H.C. reaching normal limits long after the hæmoglobin. Untoward reactions were not observed in any patient. The technique of giving the iron was that described by Slack and Wilkinson (1949).

Although most of the patients had no symptoms, after treatment a sense of well-being, more energy, and a greater interest in life were admitted by almost every patient.

Conclusions and Summary

Idiopathic hypochromic anæmia is common in young males, and is the commonest form of anæmia in R.A.F. recruits. Of 50 cases of hypochromic anæmia found among 4221 recruits, 47 could be regarded as idiopathic.

Most of the 50 patients came from large working-class families.

Symptoms were rare, even with severe anæmia.

The incidence of histamine-fast achlorhydria in hypochromic anæmia in young men, is the same as in middle-aged women with this type of anæmia. The associated histamine-fast achlorhydria was reversible in 6 of 13 cases.

Early detection and treatment of the anæmia are important for the well-being of the gastric mucosa.

The bone-marrow findings showed that the typical picture is one of moderate normoblastic hyperplasia.

Treatment with intravenous iron was safe, efficient, and reliable.

After treatment nearly all the patients experienced a sense of well-being, more energy, and more interest in life than they had been accustomed to.

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PROLONGED ANURIA

SUCCESSFUL MANAGEMENT BY CONTINUOUS INFUSION INTO THE INFERIOR VENA CAVA

C. SCOTT RUSSELL
M.A. Oxfd, M.D. Edin., F.R.C.S.E., F.R.C.O.G.
PROFESSOR OF OBSTETRICS AND GYNÆCOLOGY IN THE UNIVERSITY OF SHEFFIELD

C. J. DEWHURST
M.B. Manc., M.R.C.O.G.
LECTURER IN OBSTETRICS AND GYNÆCOLOGY IN THE UNIVERSITY OF SHEFFIELD

J. C. BRACE
M.D. Lond., M.R.C.O.G.
RECENTLY REGISTRAR, DEPARTMENT OF OBSTETRICS AND GYNÆCOLOGY, CITY GENERAL HOSPITAL, SHEFFIELD

SUDDEN suppression of urine is of such varied ætiology that few clinicians have not observed it and been required to treat it. A few cases may be caused by obstruction of the urinary tract, but most are the result of shock during which renal damage develops. If cortical necrosis is complete, the prognosis is hopeless; but this must never be assumed, because, if the lesion is less extensive and the main damage is to the renal tubules, the outlook is quite good provided the appropriate treatment is started promptly and given with care and attention to detail.

Suppression of urine often develops when least expected and when treatment is very properly being directed towards the resuscitation of the shocked patient. Herein lies a danger. In his concern to restore and maintain an adequate circulation the doctor may miss by many valuable hours the early diagnosis of anuria and (of far greater importance) by over-enthusiastic intravenous therapy may so disrupt the patient's fluid and electrolyte balance as to prejudice ultimate recovery from the anuria. In such cases, and in some others deteriorating under treatment, complicated procedures—e.g., exchange transfusions (Dausset 1950), peritoneal dialysis (Frank et al. 1948), and the use of the artificial kidney (Kolff 1952)—may be required; but, even so, conservative treatment by restriction of fluids and a high-calorie diet containing little or no protein will be required.

When anuria is diagnosed at its onset, conservative treatment should be all that is required to allow the kidneys to recover. This treatment, though properly called conservative, must not be thought of as meaning therapeutic inactivity; it is rational and demands attention to detail for which "doing nothing is the least suitable epithet imaginable" (Black and Stanbury 1948).

We describe here in detail the successful management of a case of prolonged anuria (complete for 11 days, partial for a further 10 days) following septic abortion treated in a gynæcological ward of a general hospital. We believe that the methods adopted can easily be used by others who may encounter a similar case. The feature of the treatment to which we draw particular attention was continuous infusion through a catheter in the inferior vena cava for 17 consecutive days.

Case-record

A 3-para married woman, aged 31, was admitted in the early hours of April 1, 1953. She had last menstruated 17 weeks previously, and just over 2 months later she tried to procure abortion by taking 60 or more "corrective capsules" over a period of days. Violent purgation and vomiting followed but not abortion. So she syringed herself with a soap solution on the night of March 31 and was admitted to hospital some hours later.

On admission her general condition and physique were good, her temperature was 99·4°F, pulse-rate 100, and blood-pressure 110/75 mm. Hg. Her tongue was moist and clean, and her heart and lungs showed no fault. The size of her uterus, which was tender, was compatible with a 17-week pregnancy; the cervix admitted a finger-tip, and there was some fresh blood on the examining finger. The initial diagnosis was threatened abortion.

Later the same morning, coincident with the expulsion of the gestation sac, there was much vaginal bleeding, which was soon controlled by the injection of ergometrine 0·5 mg. The systolic blood-pressure fell to 90 mm. Hg, but after a transfusion, given without reaction, of one pint of whole citrated blood it rose again.

At operation at 12·45 P.M. the same day the cervix was found to be widely open, permitting the digital removal of several portions of offensive placental tissue. No curette was used, and bleeding was slight. At the operation a small quantity of bloodstained urine was obtained by catheter.

Immediate Postoperative Stage.—The patient soon regained consciousness and showed no signs of shock. Her pulse-rate was 100 and temperature 99·4°F. She had been started on a course of penicillin 600,000 units 12-hourly and sulphadimidine, but the latter was discontinued after 2 g. had been given, in view of the urinary findings at operation.

1st Postoperative Day.—The patient's general condition was unaltered, but suprapubically the abdomen was tender and slightly rigid; the temperature and pulse-rate were unchanged. During the first 24 hours 105 oz. of fluids was estimated to have been taken by mouth, and 16 oz. to have been lost in vomit; 17 oz. of bloodstained urine, most of which had been secreted early in the day, was passed.

2nd Postoperative Day.—During this day only 4 oz. of urine was secreted, confirming the suppression of urine; this was complete by 9 P.M., when catheterisation showed that the bladder was empty. During this day the fluid intake was restricted to 30 oz.

3rd Postoperative Day.—Cystoscopy and ureteric catheterisation revealed no mechanical obstruction; 5 drops of heavily bloodstained urine was obtained from the right ureter, and none from the left. The urine was sterile on culture and contained several hyaline casts. A Ryle's tube was passed through the nose into the stomach, and an emulsion of glucose 400 g., peanut oil 100 g., and acacia to emulsify in 1 litre of water as recommended by Bull et al. (1949) was dripped slowly day and night. Vomiting occurred once, but most of this was strained through gauze and returned to the intragastric drip.

4th Postoperative Day.—A gastric drip was continued although vomiting occurred on several occasions.

5th Postoperative Day.—Vomiting had by now assumed serious proportions and was causing the patient distress and

TABLE II—BIOCHEMISTRY OF BLOOD-SERUM

Postoperative day	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27
Non-protein nitrogen (mg. per 100 ml.)	135	..	190	185	240	..	190	220	..	234	220	280	240	254	260	..	240	320	320	380	160	190	..	220	185
Sodium (mg. per 100 ml.)	295	..	275	295	290	..	..	290	..	270	270	275	280	310	..	..	285	270	270	270	..	290	..	285	..
Potassium (mg. per 100 ml.)	21	..	22	22	21	..	..	22	..	22	21	18	19	20	..	..	19	22	21	20	..	19	..	20	..
Chlorides as chlorine (mg. per 100 ml.)	..	..	..	330	323	..	..	330	..	220	220	240	300	255	17	..	280	290	315	280	..	280	..	..	..
Alkali reserve (vol. %)	..	..	..	62	..	..	..	60	..	52	54	57	59	58	..	..	60	58	61	58	62	61	..	..	..

ourselves anxiety. In the previous 48 hours she had absorbed little more than 1 litre of the mixture and was noticeably more drowsy. A sensitisation rash, which we assumed was due to penicillin, made its appearance on the thighs, abdomen, and arms, but fortunately the irritation it caused was rendered less disturbing by the patient's continued desire to sleep. A litre of 5% dextrose in water was rapidly infused to restore the fluid balance, and in an attempt to stop vomiting the stomach was washed out with water, and a dilute glucose solution was substituted for the previous mixture. Since no improvement followed, we abandoned all further attempts at gastric feeding.

6th Postoperative Day.—The problem now was how to provide the patient with the necessary calorie value without exceeding a daily fluid intake of 1 litre. Obviously a very hypertonic 40% dextrose solution could not be introduced into a peripheral vein without producing thrombosis and localised œdema. The patient's temperature had been normal for 2 days, and we did not wish to make matters worse by adopting measures which were certain to lead soon to inflammation with its dangers of increased tissue breakdown (Borst 1948). We therefore introduced a cardiac catheter as far as the superior vena cava and dripped through it a 40% dextrose solution day and night, as recommended by de Keyser et al. (1949) and Bull (1952). This provided the patient with at least 1600 calories a day and a basic fluid allowance of 1 litre to offset the insensible loss. At the same time in each 24-hour period the volume of fluid lost by vomiting was accurately measured and balanced by addition to the intravenous infusion of an equal volume of 5% dextrose in water.

TABLE I—INTAKE AND OUTPUT

Postoperative day	Intake: Oral fluids (ml.)	Dextrose 40% I.V. (ml.)	Dextrose 5% I.V. (ml.)	Physiological saline solution I.V. (ml.)	Sodium chloride 2% I.V. (ml.)	Insulin (units)	Total intake (ml.)	Chlorides as sodium chloride (g.)	Output: Vomit (ml.)	Urine (ml.)
1	2982	..	..	..	..	..	2982	..	454	483
2	852	..	..	..	..	..	852	..	..	114
3	1306	..	..	..	..	..	1306	..	960	..
4	994	..	..	..	..	..	994	..	600	..
5	994	..	1000	..	..	..	994	..	300	..
6	..	800	200	..	..	..	1000	..	210	..
7	..	800	200	..	..	..	1000	0·4	45	..
8	..	800	200	..	..	..	940*	0·6	185	..
9	..	800	200	..	..	..	835*	0·7	150	..
10	..	800	200	..	..	30	800*	3·0	270	..
11	..	800	200	..	..	30	890*	1·4	278	..
12	..	800	200	..	..	60	886*	1·3	225	..
13	..	800	..	..	200	60	1000	1·3	145	..
14	..	800	800	..	400	40	2000	3·2	265	700
15	227	800	200	..	..	40	1227	0·9	65	250
16	227	800	..	200	..	40	1227	0·8	..	220
17	170	800	..	200	..	40	1170	1·4	71	239
18	..	800	800	400	..	40	2000	4·1	310	590
19	..	800	1800	400	..	40	3000	3·7	465	280
20	..	800	1200	1000	..	70	2000	4·9	442	850
21	..	800	1600	600	..	60	2000	4·8	..	960
22	..	800	1200	1000	..	40	3000	7·9	125	1520
23	..	800	1200	1000	..	..	3000	10·9	162	1950
24	..	800	500	1200	..	..	2500	11·7	154	2520
25	284	800	..	1200	..	..	2840	12·8	..	2560
26	+ + +	400	..	600	..	..	+ +1000	13·9	..	2790
27	Intravenous therapy stopped									

During the first five days the recorded quantities of oral fluids and vomit are approximate.
Vitamins given from 23rd day onwards.
*On these occasions the bottles were changed before they were quite empty; hence the intake did not quite amount to 1000 ml.

10th Postoperative Day.—After 4 days' continuous intravenous therapy, during which the patient remained cheerful and surprisingly well in view of the continued vomiting of small quantities of fluid, thrombophlebitis was noticed along the left basilic vein, with pain, œdema, and reddening of the arm, but unaccompanied by febrile reaction. The catheter was therefore withdrawn on the 4th day of its use and with it a six-inch length of sloughing intima which we presumed had come from the basilic vein. Had the catheter not been withdrawn, the infection would probably have spread to the greater veins of the neck, with serious consequence to the patient (de Keyser et al. 1949). Since the right basilic vein had previously been marred by an unsuccessful attempt to introduce a cardiac catheter, an alternative route had to be considered. The inferior vena cava was chosen; so the right saphenous vein was exposed in the femoral triangle and a 'Polythene' catheter was introduced to a distance of 8 inches. For the next 17 days the patient received fluids and nutrition by this route without any complications arising; and, when the time came to discontinue this form of therapy, the infusion was working as perfectly as it did on the first day of its use. From this day until the 22nd postoperative day insulin was given by subcutaneous injection (table I).

14th Postoperative Day.—The patient passed 700 ml. of dark murky urine, sp. gr. 1·014, containing numerous red cells, pus, and squamous epithelial cells but no casts or crystals. Her general condition was remarkably good, as it had been throughout the anuric phase, but in the evening she became drowsy and had a febrile reaction with a mild rigor. Her skin was dry, and she complained that her tongue "tasted salty." Next day she was once again free from symptoms, but her temperature rose to 100°F during the succeeding two evenings. Vomiting persisted, and it was therefore necessary to persevere with intravenous therapy.

16th Postoperative Day.—Since the amount of hæmoglobin had decreased to 48%, a pint of group-O rhesus-positive packed cells was transfused.

17th and 18th Postoperative Days.—Cautious attempts were made to introduce water and fruit juices by mouth, but this provoked increased vomiting, wherefore we postponed further attempts at giving nourishment orally.

22nd Postoperative Day.—The non-protein-nitrogen level reached its peak at 380 mg. per 100 ml. despite an increase in daily output of urine. About now the patient began to complain of generalised severe pain, principally in the right hypochondrium and in the lumbar regions, for which we could find no cause. Possibly these symptoms were related to renal recovery.

23rd Postoperative Day.—The daily output of urine had almost reached 2 litres, and from now onwards diminishing nitrogen levels in the blood were recorded. The extent of the fall in the level of non-protein nitrogen in the serum on this day (table II) is remarkable but coincides with a reawakening of intestinal function, which up till then had been in complete abeyance. The first motion passed resembled an ordinary constipated stool, but thereafter, and until oral nourishment was resumed, fæcal material similar in appearance to meconium was passed in small quantities twice or three times a day. Once again a mild febrile reaction developed, although the patient continued to feel well.

26th Postoperative Day.—Since vomiting had ceased the day before, the patient was encouraged to take nourishment by mouth. At first we only allowed her to sip small amounts of water, soup, and fruit juices, but a more solid diet was gradually introduced over 2–3 weeks.

27th Postoperative Day.—Intravenous therapy was discontinued after 21 days.

The patient's return to health was rapid and uneventful, and 4 weeks later (7 weeks after admission to hospital) she was discharged home. Renal recovery was not yet complete,

for the specific gravity of the urine was low at 1·008–1·010, and the non-protein-nitrogen level in the blood was 72 mg. per 100 ml.

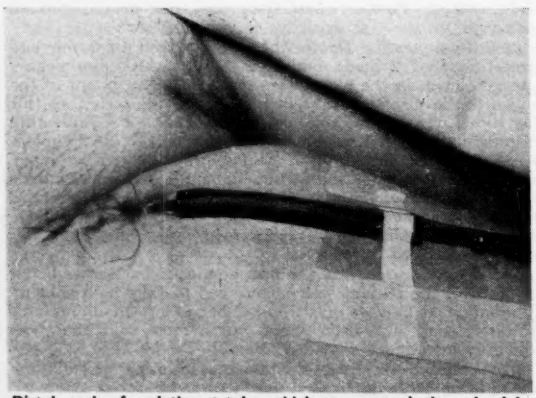
Discussion

The conservative management of anuria has been discussed by Bull (1952), Darmady (1952), and Vest and Kelley (1953), and considerable agreement has been reached on the principles of treatment. It is generally accepted that the anuric patient should be provided with at least 1600 calories a day, to reduce to a minimum the endogenous breakdown of tissues, together with water up to but not exceeding 1 litre, just sufficient to replace the insensible loss. Usually these provisions can be given in the form of an emulsion of glucose and peanut oil in 1 litre of water dripped through an intragastric tube, the technique advocated by Bull et al. (1949). In many cases this form of treatment, though unpleasant for the patient, is tolerated well and is successful, even though on occasion some of the emulsion may be vomited, when it has to be strained back into the intragastric drip. Repeated vomiting or diarrhœa is more serious, though urea and potassium are said to be lost by these routes. In the present case the continued vomiting may have helped towards recovery by getting rid of these substances.

Only when the vomiting becomes persistent will intragastric feeding have to be stopped and be superseded by intravenous therapy. Since only 1 litre of fluid in each 24 hours is permissible, and since this must provide 1600 calories, the concentration of sugar solution, if such a solution is to be chosen, must be at least 40%. Such a solution cannot, however, be run into a peripheral vein for more than a day or so without producing thrombosis; so one of the great veins must be chosen for the infusion if the drip is to be given for any great length of time. The infused hypertonic solution is apparently so quickly diluted by the blood-flow in the large vein that no thrombus is formed. From our limited experience and from discussing this matter with those of our colleagues who are accustomed to cardiac catheterisation we believed that this procedure need not be looked on as formidable or dangerous. Several technical details, however, require further consideration.

PREVENTION OF THROMBOPHLEBITIS

Unless thrombophlebitis is successfully prevented, it may not be possible to continue the only treatment likely to preserve the patient's life. The most scrupulous asepsis must be practised in putting up the drip; and this asepsis must be maintained all the time that the drip is in use. Heparin 15,000 units per 24 hours and penicillin should be added to the infused fluids. Two other factors may help to reduce the incidence of thrombophlebitis: (1) the amount of movement permitted at the point of entry of the catheter and throughout its length should be reduced to a minimum; and (2) the length of vein of small calibre traversed by the catheter should be as short as possible. Infusion into the inferior vena cava has these two merits; therefore we recommend this route rather than the alternative route, into the superior vena cava. If signs of inflammation develop despite these precautions, the catheter must be withdrawn without delay.



Distal end of polythene tube which was passed through right saphenous vein into inferior vena cava, and through which continuous infusion was maintained for seventeen days without producing any complication.

INFUSION INTO INFERIOR VENA CAVA

To minimise the risk of infection masks, gowns, and gloves should be worn and full asepsis and antisepsis practised.

The apparatus required is the same as for cutting down on a vein; a transfusion bottle containing the appropriate solution; a polythene catheter 4 mm. in diameter and about 12 inches long; a short piece of thick-walled rubber tubing to fit tightly over the polythene tube; and all connecting pieces (see figure).

A 2-inch incision exposes the upper end of the saphenous vein, whose three or four main tributaries and distal end are carefully ligated. The vein is opened and the polythene catheter passed for 8–10 inches and secured firmly with a double ligature of fine catgut. The following arrangement exerted pressure on the wound not only while the catheter was in situ but also when the time came for it to be removed.

At the time of insertion of the catheter a stout nylon suture (size 8) was passed through the skin, under the saphenous vein $^1/_2$ inch proximal to the point of entry of the catheter, over the vein, and then under it once more, and brought out through the skin on the opposite side. This suture was securely tied over a small pad of sterile gauze, with its ends left long. When the time came to remove the catheter, the nylon knot over the gauze was loosened; as soon as the catheter was withdrawn, the suture was tightened over the gauze pad rather more firmly than before; this kinked the saphenous vein, thus preventing hæmorrhage. The nylon suture was removed by firm traction 72 hours later.

Specimens of blood for biochemical analysis may readily be collected through the polythene tube by temporarily stopping and disconnecting the drip and aspirating blood with a syringe. When the drip is reconnected, as much as possible of the blood remaining in the tube should be flushed back into the circulation without delay by momentarily racing the drip; otherwise a thrombus may form in the tubing.

INFUSION INTO THE SUPERIOR VENA CAVA

For catheterisation of the superior vena cava certain additional points in technique must be observed. The catheter should be of the type normally used for cardiac catheterisation; the median antecubital vein, preferably the right, is exposed and the catheter inserted first into the basilic vein, thence into the subclavian vein, and onwards under the fluorescent screen into the superior vena cava. Sometimes the tip of the catheter enters the wrong vein, especially the internal jugular vein. When this happens, it should be partially withdrawn and the patient's arm abducted and rotated before the catheter is reinserted. The tip of the catheter should not remain in either the jugular or the subclavian vein, because the continued use of hypertonic solutions may cause them to thrombose (de Keyser et al. 1949).

CONTROL OF INTRAVENOUS THERAPY

In the present case 1 litre of 40% dextrose was infused daily together with such additions as were required to make up fluid lost in vomit or urine. For convenience, the additions consisted of 5% dextrose in water.

The correction of electrolyte deficiency during anuria is not normally practised (Bull et al. 1950) and therefore we were reluctant to give saline solution, but after a very careful day-to-day tally of the amounts of sodium chloride lost by vomiting it became clear on the 14th postoperative day that a real deficit amounting to nearly 9 g. existed. Moreover, at this time the sodium and chlorine levels in the serum were somewhat lower than they had been; therefore 4 g. of sodium chloride was added to the dextrose drip. Next day diuresis began, and thereafter we had no hestitation in adding to the

infusion amounts of saline equal to, but never in excess of, the chlorine and sodium deficit at the time.

Table II shows that the serum-potassium level during the anuria remained at fairly constant low values and never exceeded 22 mg. per 100 ml. Small amounts of potassium chloride were introduced into the drip on three occasions during the recovery period, during which the serum-potassium levels fluctuated from 17 to 22 mg. per 100 ml.

Ketosis and acidosis did not develop—a fact which is all the more remarkable when it is remembered that for 3 weeks the patient was given nothing by mouth and throughout this time vomiting continued without respite.

HANDLING OF BIOCHEMICAL DATA

Since the patient's life appeared to depend on the careful recording and assessment of biochemical results, and on a meticulous regard to detail in many small but important practical matters, the following programme of management was evolved.

Samples of blood with the 24-hour collections of either urine or vomit or both were dispatched for analysis each day at 9.30 A.M. The laboratory findings in these specimens were telephoned back to the ward by 2·30 each afternoon; and all results so notified were received and recorded immediately either by one of us (J. C. B.) or by the ward sister.

Biochemical and fluid deficits were calculated from the daily laboratory results, and from these the nature and amount of extra parenteral fluid therapy for the succeeding 24-hour period was estimated. For convenience this 24-hour period always began at 3.30 P.M.

Except for a few days, one of us (J. C. B.) accepted the responsibility for the close handling and scrutiny of the biochemical data, and for the control of the intravenous therapy. This arrangement was an important factor leading to our patient's recovery.

Summary

The principles to be adopted in the treatment of anuria are briefly considered.

The successful management of prolonged anuria (complete for 11 days, partial for a further 10 days), following septic abortion is described in detail.

The limitations of oral feeding for anuric patients with gastric intolerance are emphasised. In the present case excessive vomiting precluded the continuation of feeding by intragastric tube. The patient's nutritional requirements were effectively supplied for 21 days by the intravenous administration of dextrose 400 g. daily. Over-hydration was prevented by infusing a 40% solution of dextrose at first into the superior vena cava and later into the inferior vena cava.

The two techniques of infusion into the superior vena cava and into the inferior vena cava are neither difficult to perform nor particularly distressing to the patient. For reasons discussed here we prefer infusions into the inferior vena cava, and in the present case we maintained the infusion into this vein for 17 consecutive days without complication.

We believe that infusion of a 40% glucose solution into one of the great veins may have a wider application than hitherto in the treatment of patients who cannot obtain nourishment through the alimentary tract; but this method may not achieve what is hoped for it, unless the electrolyte and fluid balance is carefully assessed daily and close attention is given to the management of the infusions. If this can be done by one and the same person, so much the better.

We wish to thank Mr. F. J. P. O'Gorman, F.R.C.S., for his cystoscopic examination of our patient, Mr. B. W. Auchinachie, PH.D., and his staff for the daily biochemical analyses, and Dr. F. W. Leigh, of the cardiovascular department of the Hospital, for his assistance with the intravenous infusions, and Sister Mitchell and the nurses for their invaluable help.

References at foot of next column

METHONIUM COMPOUNDS IN THE ANGINA OF HYPERTENSION

A. E. DOYLE, M.D. Lond., M.R.C.P.
LECTURER IN CARDIOLOGY

J. A. KILPATRICK, M.D. N.Z., M.R.C.P., M.R.A.C.P.
LECTURER IN MEDICINE

OTAGO UNIVERSITY MEDICAL SCHOOL, DUNEDIN, NEW ZEALAND

THE careful administration of hexamethonium bromide (H.M.B.) and its homologues is probably the most effective treatment at present available for arterial hypertension, and with it a great measure of improvement may be obtained in almost all patients. Papillœdema, where present, disappears in almost all adequately treated cases, and reduction in heart size is common (Smirk 1953b and c). Improvement can be seen in the electrocardiograms in most cases (Doyle 1953). In most cases, congestive heart-failure or left ventricular failure can be relieved without the use of digitalis, mersalyl, or salt-free diet (Smirk 1953c).

Many hypertensive patients suffer from angina pectoris. In some series the proportion is as high as 20% (Schottstaedt and Sokolow 1953), while 13% of the 1264 hypertensive patients reviewed by Goldring and Chasis (1944) died of coronary thrombosis.

Hayward (1952) has suggested that the reduction of aortic diastolic blood-pressure produced by effective treatment with the methonium compounds may lead to a decrease in coronary blood-flow, and hence to myocardial ischæmia or to cardiac infarction. Morrison (1953) preferred not to use these compounds in treating hypertensive patients with angina. There is some evidence that myocardial ischæmia may sometimes follow reduction of the blood-pressure. Lindgren and Frisk (1948), for example, reported prolonged precordial pain in 3 anginal patients and coronary thrombosis in a 4th after the blood-pressure had been reduced by tetraethylammonium chloride. In an earlier publication from this department (Smirk and Alstad 1951) it was reported that methonium salts should be administered to anginal patients very cautiously, but that improvement was detectable in some patients.

Test injections of H.M.B. or similar substances have now been given here to over 450 patients, of whom 250 have been treated for long periods. Of the 450 patients who have had test injections, 50 had angina pectoris. 40 of these have been treated for three months or more with a methonium compound.

We report here the effects of test injections and prolonged treatment in these hypertensive patients with angina, with particular reference to spontaneous chest pain resulting from reduction of blood-pressure and the effects of treatment on the severity of the angina.

Case-numbers correspond with those in earlier publications (Smirk and Alstad 1951, Kilpatrick and Smirk 1952, Doyle 1953).

Methods

Selection of Patients

All patients with angina whose casual systolic blood-pressure was over 160 mm. Hg and who received test injections of H.M.B. or related compounds have been included in this series, and all such patients who were

PROF. SCOTT RUSSELL AND OTHERS: REFERENCES

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referred to the clinic have been tested to avoid errors of selection. Angina was diagnosed by one of us, and where there was doubt separate opinions by each have been obtained. Only patients in whom the pain was agreed to be undoubtedly anginal have been included in this series.

Method of Treatment

Patients were weighed at each attendance. No form of therapy was given until a methonium compound had been tried. Test injections were made subcutaneously and the blood-pressure was recorded in the standing and sitting positions at half-hourly intervals. Treatment in most patients has been by subcutaneous injection of H.M.B. Oral treatment was effective in 13 patients, and these were given hexamethonium bitartrate by mouth or 'M. & B. 2050A' by mouth. A few have been treated with M. & B. 2050A by subcutaneous injection (Smirk 1953a). The initial dose of H.M.B. used was 7·5 mg., while the initial subcutaneous dose of M. & B. 2050A in polyvinylpyrrolidone (P.V.P.) was 2 mg. The initial dose of M. & B. 2050A by mouth was 20–40 mg. Our methods of control of treatment with these substances have been described elsewhere (Smirk 1953b). In treating patients with angina we have taken additional precautions. Initial doses were half of those usually given to other hypertensive patients. The dose was then raised daily with close supervision until a dose was reached which reduced the systolic blood-pressure in the standing position to about 140 mm. Hg, provided that there had been no spontaneous chest pain before this point was reached. Careful watch was kept for such pain, and immediately it was felt the patient was made to lie down. This relieved the discomfort at once. Spontaneous chest pain associated with falls in blood-pressure was always regarded as indicating that the limit of safe dosage and of blood-pressure reduction had been exceeded. Occasional mild attacks of spontaneous chest pain were regarded as an indication, not for stopping treatment but rather for reducing the dose.

Results

SEVERITY OF ANGINA

Of 50 patients with definite angina, 10 refused, or were thought unsuitable for, prolonged treatment. The remaining 40 patients have been treated with one of the methonium compounds for three months or more. The longest period of treatment has been three and a half years. The average time of treatment for the 40 patients was ten and a half months.

In 11 of the 40 patients the pain has disappeared altogether, and all of these patients are much more active than before treatment was given.

In a further 22 patients the severity of the angina has been reduced, so that most are able to take more exercise with less frequent pain. Several have returned to work, and some have been able to lead almost normal lives.

The remaining 7 patients were unimproved by treatment.

The effort tolerance did not appear to be reduced in any of the patients treated. Those in whom spontaneous chest pain developed are referred to below.

Improvement in the angina is rare with less than about a week's treatment and may not take place for up to a month. Benefit is usually greatest by the end of the third or fourth month of treatment, and further improvement after this period is unusual Relapses of pain do not seem to occur provided that doses producing adequate falls of blood-pressure continue to be taken.

Accuracy of dosage is most important, since doses which cause excessive falls of blood-pressure may produce spontaneous chest pain, while doses followed by ineffective falls of blood-pressure do not often improve the effort tolerance.

The following are some of the cases in which improvement took place.

Case 343.—A man, aged 66, was first seen in November, 1952. There had been severe angina of effort for three months, but no protracted attack of pain. For several years he had had headache and giddiness and there had been some dyspnœa on exertion. The blood-pressure was 200/120 mm. Hg; the fundi showed grade-II changes (Wagener and Keith 1939); the electrocardiogram showed grade-III (advanced hypertensive) changes (Doyle 1953); and radiography showed no cardiac enlargement.

Treatment was started in January, 1953. Within a week his effort tolerance was considerably improved, and the patient could walk very much further with less frequent pain. The improvement continued, and when seen in May he said that his activity had returned to normal and there had been no further pain. He was seen again in July, when he said that there had been some recurrence of pain after he had reduced the dose because of dryness of the mouth. On restoring the dose to its previous level the pain disappeared again. When last seen (in October) he was free of pain and was more active than before treatment.

Case 52.—A woman, aged 45, was first seen in June, 1948, with a blood-pressure of 248/140 mm. Hg. She complained of severe headaches of many years' duration, attacks of giddiness, and shortness of breath and anginal pain on effort for the past year. The heart was much enlarged; and there were many retinal hæmorrhages, some exudate, retinal œdema, and an ill-defined edge to the disc. She was admitted to hospital in December, 1949, when the blood-pressure was 260/180 mm. Hg. There were frequent attacks of left ventricular failure and breathlessness at rest, and she was almost bedridden. There was advanced papillœdema. The angina had been severe for two and a half years.

Treatment with H.M.B. was started. Within two months headache, breathlessness, and the dizzy attacks had disappeared, and within six months the papillœdema had cleared. Until April, 1951, the patient lived a substantially normal life, apart from the injections, and had no chest pain or breathlessness with moderate activity. She died in April, 1951, of a cerebral hæmorrhage. Post-mortem examination showed that the heart was much enlarged (weight 575 g.), the enlargement being almost entirely due to left ventricular hypertrophy. The coronary arteries were widely patent, and although there was some concentric intimal thickening there was no gross atherosclerosis. There was no evidence of myocardial infarction.

Case 704.—A woman, aged 66, was admitted to the Dunedin Hospital in April, 1953. She had had typical angina for fifteen years, and for the last year the attacks had come on with the slightest exertion and sometimes in bed. The electrocardiogram showed grade-III changes; the basal blood-pressure was 222/124 mm. Hg, and radiography showed considerable left ventricular enlargement.

Treatment was started with M. & B. 2050A in P.V.P. by subcutaneous injection. The patient was last seen in September, 1953. Since treatment had been begun there had been two long attacks of severe precordial pain starting in the early hours of the morning. These were associated with attacks of abnormal rhythm which the electrocardiogram showed to be ventricular tachycardia. Generally speaking, she was much improved. There had been no other attacks of pain at rest, and she could do considerably more with less frequent pain.

Case 708.—A woman, aged 46, was first seen in September, 1950, with a history of angina of effort for eighteen months. The pain came on with slow walking up a slight hill. The casual blood-pressure was 210/130 mm. Hg. The electrocardiogram was normal at rest but showed distinct depression of the S–T segment in the left-sided precordial leads after exertion.

The patient was treated with hexamethonium bitartrate by mouth, and doses of 1 g. reduced her blood-pressure to about 140/90 mm. Hg. She was last seen in October, 1953, when there was no pain on ordinary activity; she could walk up moderate hills and ride a cycle to work without pain. The electrocardiogram had not improved.

Case 712.—A man, aged 55, was first seen in the outpatient department in March, 1953. He had had angina of effort for six weeks. There had been no severe attack, but the electrocardiogram showed right branch bundle block with distinct S–T-segment depression over the left-sided precordial leads.

Treatment was started in June, 1953; and he was last seen in October. At this time he said that he still had pain on hills and on the level against a wind. He could ride some three-quarters of a mile on a bicycle before the pain came on, whereas before treatment he could not do more than two hundred yards. Although clinical improvement was considered to be doubtful and the electrocardiographic pattern of right branch bundle block was unchanged, the S–T-segment depression previously present had disappeared. Treatment was difficult in this patient because of spontaneous pain when the systolic blood-pressure fell below about 150 mm. Hg.

SPONTANEOUS CHEST PAIN

Of the 50 patients with angina who have had test injections or prolonged treatment, 13 had spontaneous chest pain during the period of blood-pressure reduction. In addition, a further 2 patients who had never previously noted angina had spontaneous anginal chest pain when the blood-pressure was reduced. We believe that the smallness of the proportion of patients who have had such spontaneous pain is largely due to careful supervision of treatment.

The blood-pressure level at which spontaneous pain develops varies from patient to patient. Most do not get spontaneous pain unless the systolic blood-pressure falls below about 120 mm. Hg; but in some patients (for example cases 712 and 143) spontaneous chest pain occurred at rather higher levels, case 143 complaining of pain when the systolic pressure fell to 180 mm. Hg. In 2 patients spontaneous chest pain has occurred in association with paroxysmal tachycardia—in one of ventricular type, in the other of auricular type. We have had the impression that spontaneous pain is more likely in the early stages of treatment, although it may occur at any stage if doses causing excessive falls of blood-pressure are given. In some patients the pain seems to be caused by the abrupt falls of blood-pressure, and this may occasionally be avoided by giving oral preparations or slowing agents to delay the fall of blood-pressure (Smirk 1952). In some patients, however, the effects of oral administration are too unpredictable for accurate control of treatment, since capricious alimentary absorption may lead to occasional excessive falls of blood-pressure.

Treatment had to be discontinued in 5 patients (cases 139, 143, 176, 197, and 719) because of spontaneous chest pain.

Case 139.—A woman, aged 67, was admitted to the Dunedin Hospital in February, 1951, with a history of dyspnœa on exertion for four years and angina of effort for three years. On clinical examination there was moderate cardiac enlargement. The casual blood-pressure was 190/130 mm. Hg. The electrocardiogram showed grade-III changes

Treatment with oral hexamethonium bitartrate was begun, but this had to be discontinued after a month because of diarrhœa, and treatment by subcutaneous injection was substituted. There was slight improvement in the severity of the angina after two months' treatment, but at the end of this time the patient had a long attack of chest pain. It was thought that this attack probably followed an overdose of the drug since the patient had not understood the instructions for dosage. The treatment was discontinued because of the onset of presenile dementia.

Case 143.—A woman, aged 53, was admitted to the Dunedin Hospital in February, 1951. She had been treated for angina of effort for five years, and cardiac infarction had occurred four years previously. On admission there was clinical and radiographic evidence of gross cardiac enlargement. The casual blood-pressure was 268/130 mm. Hg, and the basal blood-pressure was 210/118. The electrocardiogram showed grade-III hypertensive changes.

A subcutaneous injection of 20 mg. of H.M.B. reduced the blood-pressure to 196/98, at which level the patient complained of pain in the chest. An injection of 0·9% saline the next day also produced an attack of pain with the blood-pressure at 218/106 mm. Hg. Treatment was discontinued because of the ease with which pain occurred and because the patient was particularly apprehensive and suggestible.

Case 176.—A man, aged 49, was first seen in 1946 with angina of effort following a myocardial infarction. The angina persisted, and he was seen again in July, 1951. The casual blood-pressure at this time was 210/120 mm. Hg. It was decided to assess the effects of H.M.B.

The blood-pressure could be reduced to 116/90 mm. Hg without the development of spontaneous chest pain. With administration of H.M.B. there seemed at first to be some subjective improvement, but at the end of two months the angina was substantially as severe as before. At about this time the patient had a severe attack of spontaneous chest pain, and, since improvement had been slight, treatment was discontinued. He continued to have angina until his death from another cardiac infarction fifteen months after stopping treatment. Necropsy revealed severe coronary sclerosis with a recent anterior myocardial infarction and an old posterior infarction.

Case 197.—A woman, aged 58, was first seen as an outpatient in May, 1951, with complaints of headache and giddiness. There was no angina at this time. The casual blood-pressure was 250/140 mm. Hg. There was no clinical evidence of cardiac enlargement, and the fundi showed grade-II changes. The basal blood-pressure was 162/114 mm. Hg. The electrocardiogram showed advanced hypertensive changes.

Treatment by subcutaneous injections of H.M.B. was started in August, 1951, but a month later the patient was readmitted after a long attack of chest pain which was due to coronary insufficiency; the pain had come on six hours after the last injection of H.M.B. Treatment was discontinued at this time, but the patient was readmitted in December, 1951, with congestive heart-failure. The casual blood-pressure at this time was 212/152 mm. Hg. The failure was rapidly overcome by administration of H.M.B., and this treatment was continued without further incident until May, 1952. At this time the patient was readmitted with severe bronchopneumonia. Treatment was again discontinued and was not subsequently recommenced. She died in September, 1952, of a cardiac infarction. There was no necropsy.

Case 719.—A woman, aged 42, was seen as an outpatient in January, 1953, with a history of angina of effort for three years and of cardiac asthma for three months. The casual blood-pressure was 175/110 mm. Hg. There was no clinical or radiographic evidence of cardiac enlargement, and the electrocardiogram at rest was normal, although there was depression of the S–T segment in the left-sided precordial leads after exercise.

Treatment with oral hexamethonium bitartrate was started. There appeared at first to be some improvement, but this was never very great. Three months after treatment was started severe diarrhœa developed, and treatment with subcutaneous H.M.B. was substituted. The patient proved extremely sensitive to the drug, and $7\frac{1}{2}$ mg. subcutaneously reduced the blood-pressure to 110/70 mm. Hg and spontaneous chest pain occurred. In view of doubt about the improvement and the spontaneous chest pain, treatment was discontinued. The angina has since persisted.

CARDIAC INFARCTION

Of the whole series of 450 patients, 10 have had cardiac infarctions. Of these, 4 were under treatment at the time of the infarction and the remaining 6 were not being treated. In each of the untreated patients the infarction was fatal. 2 of the patients who were under treatment recovered from the infarction, but both died from subsequent cardiac infarction before treatment had been recommenced. In only 1 patient did cardiac infarction occur at a time when the blood-pressure was low as the result of administration of H.M.B. In the remaining patients the pain started when the blood-pressure would normally have risen after the previous injection. We have the impression that careful treatment with these substances, producing moderate falls of blood-pressure, does not lead to cardiac infarction even in patients with angina. We have ordinarily not treated patients with these substances if cardiac infarction has occurred in the preceding six weeks.

Discussion

The normal ratio of cardiac work to coronary blood-flow is disturbed in patients with angina (Wégria 1951).

It is apparent that arterial hypertension increases the cardiac work. Blumgart et al. (1940) and Davis and Klainer (1940a, b, and c) demonstrated, in studies of the relation of the clinical manifestations of angina and myocardial infarction to the pathological findings, that some patients with clear-cut angina had normal coronary arteries, the heart being considerably hypertrophied because of hypertension or valvular disease. Harrison and Wood (1949) concluded from a study of hypertensive patients with angina that in many there was coronary dilatation rather than narrowing, so in these the main cause of the angina seemed to be increased cardiac work. In the present series some of the cases examined post mortem showed no evidence of coronary arterial narrowing.

There is little doubt that in the hypertensive patient reduction of the blood-pressure appreciably reduces cardiac work. In those patients with hypertension who obtain relief from angina after reduction of the blood-pressure, it seems probable that the reduction in cardiac work is greater than the reduction in coronary blood-flow when the aortic blood-pressure falls. In a few patients, however, with moderate falls in blood-pressure the reduction of the mean aortic diastolic blood-pressure, and hence of coronary blood-flow, may exceed the reduction of cardiac work so that spontaneous chest pain occurs. In our experience, such a sequence is unusual if the fall of blood-pressure is carefully controlled. We have had the impression, however, that if the blood-pressure is allowed to fall excessively spontaneous chest pain will occur in a larger proportion of patients. The level of blood-pressure at which such pain occurs can be determined in the individual patient only by the most circumspect increments after a small initial dose.

In practice, therefore, angina pectoris complicating hypertension need not be a contra-indication to the use of the methonium compounds. Indeed, the use of those compounds seems to be indicated, provided that they are administered very cautiously. For the ordinary hypertensive patient the fall of blood-pressure in the standing position should be such that recumbency will immediately restore the pressure to about the original level, and it is essential that this precaution be observed in treating the hypertensive patient with angina. This entails frequent observation of the patient in the preliminary period of stabilisation, and critical adjustment of dose; this can be achieved only by the use of syringes graduated to 0·01 ml. Furthermore, the standing systolic blood-pressure should not be reduced below 140 mm. Hg, at least in the preliminary period of treatment when attacks of coronary pain are commonest. We have the impression that spontaneous pain is less likely if the blood-pressure is reduced slowly by the use of delaying agents and sometimes by oral therapy. Oral H.M.B. is, however, not often successful (Kilpatrick and Smirk 1952) and even patients who can take adequate doses by mouth without prohibitive side-effects may have excessive falls of blood-pressure because of the irregular effect of administration by this route.

It has not been possible in the present series to assess the placebo action of these drugs in relieving angina. It is well known that angina can commonly be relieved by placebos. The improvement in other symptoms of hypertension after hypotensive therapy, with the induction of hypotensive symptoms, makes it difficult to substitute ineffective therapy without the patient's knowledge. The main object of treatment in our patients, however, has not been so much the relief of angina as the control of the hypertension in general; and in most cases the angina has been one of numerous symptoms. We have the impression that the striking improvement which occurs gradually over a period of several months can be more reasonably attributed to the reduction of blood-pressure than to a placebo action.

Summary and Conclusions

The methonium compounds may be safely administered to hypertensive patients with angina, with close supervision by experienced physicians and well-trained technical assistants.

The effects of reducing the blood-pressure by this means have been studied in 50 cases. About a quarter of the patients had occasional attacks of spontaneous chest pain and in 5 treatment had to be stopped because of such pain after modest falls of blood-pressure.

A third of the patients treated lost all angina after some months' treatment, while two thirds of the remainder were much improved in this respect.

Cardiac infarction was no commoner in treated patients than in similar untreated patients.

We are indebted to Prof. F. H. Smirk for much helpful advice and criticism. We wish to thank also Miss B. Hoare, Miss B. Stanton, and Miss O. Fraser without whose technical assistance at the hypertensive clinic these observations would not have been possible. We are indebted to Miss N. Richardson and Miss M. Poppelwell for secretarial help. The hexamethonium bromide and related compounds were supplied by Messrs. May & Baker Ltd., Dagenham, Essex.

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PORPHYRIA TREATED WITH NEOSTIGMINE

R. O. GILLHESPY
M.D. Edin., F.R.C.P.E.
PHYSICIAN TO THE DUDLEY ROAD GROUP OF HOSPITALS, BIRMINGHAM

S. G. SMITH
B.Sc. Birm.
BIOCHEMIST, DUDLEY ROAD HOSPITAL, BIRMINGHAM

WE have recently studied a case of porphyria combining clinical and biochemical features not hitherto described in this disease. The patient recovered after treatment with neostigmine. Successful therapy of porphyria with this drug has not previously been described.

The presenting clinical features were (1) severe colicky abdominal pain associated with nausea and vomiting; (2) dark urine; (3) progressive loss of weight producing emaciation (fig. 1); (4) progressive weakness of the limbs; (5) hoarseness; and (6) hirsuties (fig. 2).

Case-report

A woman, aged 37, was apparently perfectly well until January, 1951, when she was admitted to a general hospital in the West Country with severe generalised lower abdominal pain accompanied by nausea and vomiting. The diagnosis of acute appendicitis was not substantiated at operation, nothing abnormal being discovered. After this operation the patient lived in Jersey, and continued to have severe colicky abdominal pain, constipation, rectal discomfort, frontal headaches, and intermittent bouts of pyrexia. After returning home, and while she was working as a supervisor in a large café,

these symptoms became so severe that she was admitted to a large general hospital for investigation. In hospital she passed dark urine and her voice became husky. Nervous dysfunction of the bowel was diagnosed, and the patient was discharged. Late in September, 1951, she was readmitted to the West Country hospital. She became depressed and tried to commit suicide by taking gr. 18 of soluble phenobarbitone. She was transferred to a mental hospital and shortly after admission complained of numbness and weakness in the limbs. Electroconvulsion therapy was ordered, and immediately afterwards both legs became useless. After seven days the treatment was repeated, and next morning her arms as well as her legs were useless. Deterioration in her general condition continued, and on Feb. 9, 1952, she was taken home by her relations and within a few days was admitted to this hospital.

On examination gross emaciation of all the muscle-groups throughout the body was apparent, a thick growth of hair covered most of the body, especially the face, and there was slight exophthalmos (figs. 1 and 2). The blood-pressure was 120/90 mm. Hg. The heart-rate was increased, and the apex-beat was felt in the fifth intercostal space $3^1/_2$ in. from the midline. Nothing abnormal was detected in the respiratory system and abdomen. All the cranial nerves except the tenth were normal. Paralysis of the right recurrent laryngeal nerve caused complete inability to move the right vocal cord. The arms and legs could not be moved. The tendon-reflexes were all present, and the plantar responses were flexor. There was no impairment of sensation.

Investigations.—A full biochemical, bacteriological, and cytological examination of the cerebrospinal fluid, including a Wassermann reaction and Lange curve, revealed no abnormalities. Examination of the blood gave a normal electrolyte pattern, calcium and phosphorus, glucose-tolerance test, urea, gonococcal fixation test, and blood-count; liver-function tests were also normal, as was the calcium in urine and fæces, and the basal metabolic rate. The blood-cholesterol level was raised on admission but dropped to normal on discharge.

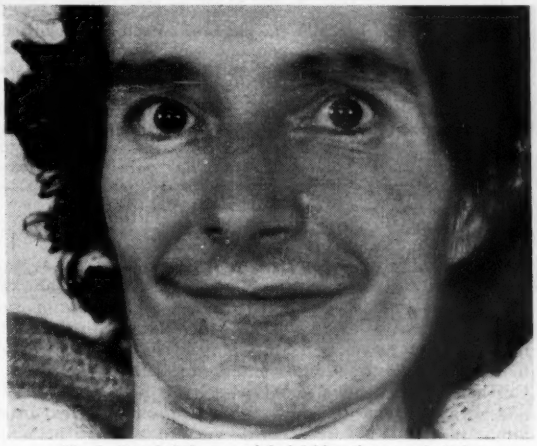

Fig. 2—Exophthalmos and facial hirsuties on admission.

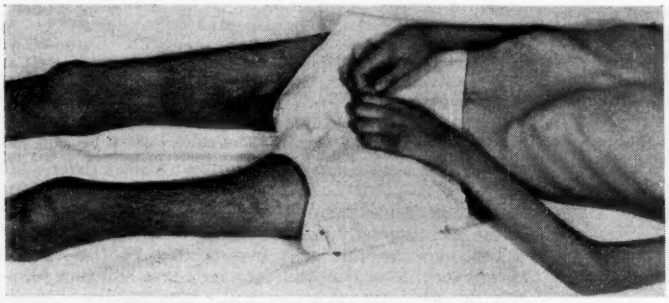

Fig. 1—Emaciation and hirsuties of thighs on admission.

Urinary creatinine excretion was somewhat depressed, whereas creatine excretion was raised. Examination of bone-marrow revealed that the erythropoietic system was active, and many macronormoblasts were seen. None of the red-cell precursors were megaloblastic. The white-cell maturation was normal. Radiography of the chest and lumbar spine showed no abnormalities, whereas radiography of the hands showed osteoporosis of the carpus and metaphyses of the bones, suggesting osteoporosis due to disuse. The electrical reaction of the muscles was normal to faradism and galvanism, and no myasthenic reaction was present. A biopsy specimen showed an increase of nuclei and small collections of lymphocytes between the muscle-fibres, with atrophy of the muscle (this is the essential appearance of myasthenia gravis). An electrophoresis pattern of the serum-proteins showed a very slightly raised gamma-globulin level.

The urine became pinkish red on standing and on treatment with hydrochloric acid, and gave a pink fluorescence in ultraviolet light. Examination of the spectrum of a 25% solution of hydrochloric acid in the urine showed bands at 5956 and 5520 A°, the spectrophotometric absorption pattern being characteristic of an acid porphyrin solution. Ehrlich's reagent gave with the fresh untreated urine a pink colour which could not be extracted with amyl alcohol. Porphyria was therefore established. The urine-uroporphyrin levels were quantitatively estimated during four phases of the patient's stay in hospital. Levels of up to 10 mg. a day were found during the first fortnight, although accurate estimates were made difficult because of the patient's bed-wetting. After two, eight, and ten months the average daily level during a week's excretion was 1·41, 2·85, and 2·11 mg. a day respectively. The peak excretion was noted during menstruation. From its behaviour in ethyl acetate solution, the uroporphyrin appeared to be type I. The urine-coproporphyrin levels were also estimated and varied between 0·1 and 1·0 mg. a day. Column chromatography of an extract from a six-day collection of fæces showed the presence of coproporphyrin plus a decarboxylic porphyrin.

Treatment of Porphyria.—The treatment of porphyria is empirical; but, since the histological picture of the muscle was similar to that associated with myasthenia gravis, neostigmine 1 mg. was injected subcutaneously three times a day, with a remarkable response. Within half an hour of the first injection the patient moved her arms and legs easily, and her voice, hitherto very hoarse and faint, became stronger and clearer. She sat up without assistance for the first time since the electroconvulsion therapy in November, 1951. This improvement gradually declined until the next dose was given. Ashby (1924), Gray (1924), Schmidt-Labaume (1926), and Mackey and Garrod (1926) reported that a megaloblastic picture is sometimes present in porphyria and that injections of liver extract proved helpful. The presence of macronormoblasts in the marrow may have been due to subnormal amounts of the liver factor; so 'Anahæmin' 2 ml. weekly was given. After a few weeks of this treatment the marrow became normoblastic. The patient's general condition improved steadily, and after a month she could sit comfortably without support on the edge of the bed and could move her right arm across the body and touch the tip of her left shoulder. As her strength increased, her ability to turn in bed returned. After seven weeks distilled water was substituted for the neostigmine, and within a few hours the muscles became stiff, and control of the arms and legs was lost. When neostigmine was given again the symptoms rapidly disappeared. After a few more weeks' therapy the voice became clear and strong, and crossing and recrossing of the legs became possible. Small

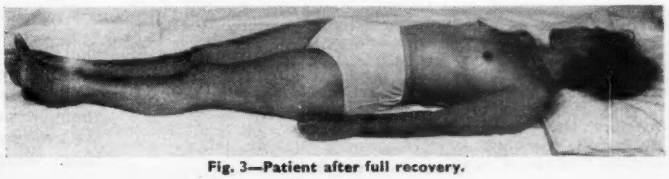

Fig. 3—Patient after full recovery.

objects could be placed in the mouth, and the patient ate without assistance. After pronation of the wrists returned, ability to write and to turn the pages of a book soon followed. Steady improvement continued, and walking with mechanical devices on the limbs began after ten months, enabling the patient to be discharged from hospital.

Follow-up.—A rehabilitation course was arranged, and tuition as a telephone operator (one of her former occupations) was given. Recently she omitted the neostigmine for four days and listlessness, acute abdominal pain, and nausea returned but quickly disappeared when neostigmine was taken again. The patient has now fully recovered (fig. 3).

Discussion

Treatment with neostigmine was tried because the histological appearance of the muscle resembled that of myasthenia gravis. The favourable result cannot be doubted, because there was an immediate improvement in the muscle power and well-being, with a relapse when distilled water was substituted for the neostigmine. Further, a relapse occurred when the patient omitted neostigmine after discharge. This favourable response might be explained by a coexistence of a constitutional defect leading to porphyria and of myasthenia gravis, the improvement being due to the influence of the neostigmine on the myasthenia. This hypothesis is supported by the fact that the patient continues to excrete as much porphyrins in her urine and fæces as before the start of therapy; but the absence of other signs and symptoms of myasthenia gravis makes this argument unlikely.

The finding of porphobilinogen in the urine leads to the diagnosis of acute porphyria, although the presence of uroporphyrin I is more in keeping with congenital or mixed porphyria.

Hirson (1953) reports two patients with acute porphyria who recovered spontaneously. Therefore the start of neostigmine therapy in the present case may have coincided with a natural remission of the porphyria, but the return of the symptoms after the withdrawal of neostigmine on two occasions is against this argument.

We therefore think that there was a response to neostigmine and urge that this drug be tried when porphyria has been diagnosed.

As in previous cases, barbiturates had been taken before acute porphyria was detected.

Physiotherapy and rehabilitation considerably helped the patient's recovery.

Summary

A patient with acute porphyria exhibited unusual clinical features, including paralysis of the left recurrent laryngeal nerve, deterioration in the clinical condition following electroconvulsion therapy, hirsuties, lymphocytic infiltration of the muscles, and the presence of uroporphyrin I and porphybilinogen in the urine.

The patient recovered when treated with 1 mg. of neostigmine given subcutaneously three times a day and later by mouth in 10 mg. doses.

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NEW LIVER-FUNCTION TEST

KARL CLOSS
Ph.D., B.M.S.
PROFESSOR OF PHARMACOLOGY, UNIVERSITY OF BERGEN
From the Central Laboratory, Aker Hospital, Oslo, Norway

THE number of so-called liver-function tests has greatly increased, and the older mercuric-chloride tests (Takata-Ara, Gros, &c.) have been superseded by more sensitive and more convenient means of discovering damage to the liver parenchyma. All these tests reveal abnormalities of the serum-proteins—e.g., in parenchymatous liver disease the γ and β globulins are usually increased and are precipitated more easily, and the albumins exert less protective action than is usual—and all have one feature in common: they give precipitations (produce turbidity or flocculation) in pathological sera but none in normal sera.

When chloranilic acid (2 : 5-dihydroxy-3 : 6-dichloroquinone), which precipitates protein, was tried in sera from different cases, including some of liver damage, it did just the opposite: it formed a precipitate in all normal sera and in all sera that gave a negative Takata-Ara test. In the sera where the Takata-Ara reaction was positive the more strongly positive the Takata-Ara reaction the less protein was precipitated by chloranilic acid, there being no precipitation at all in the most strongly positive sera.

TABLE I—INFLUENCE OF pH ON CHLORANILIC-ACID REACTION

Reagent no.*	pH of reagent	Serum no.	pH of mixture	Chloranilic-acid test
1	2·50	1	3·19	+
		2	3·18	++
		3	..	−
		4	..	−
		5	..	−
2	2·53	1	3·36	(+)
3	2·75	1	3·88	−
		2	3·83	−
4	2·44	1	2·86	+++
		2	..	+++
		3	..	+++
		4	..	+++

* 1, Usual reagent. 2, Reagent without acetic acid. 3, Reagent with 5 drops of 10% sodium-carbonate solution instead of 0·2 ml. of glacial acetic acid. 4, Reagent with 1·0 ml. of glacial acetic acid.

The new reaction was investigated in the Central Laboratory, Aker Hospital, for over a year and then taken into use as our routine method. The results obtained with this method compare very favourably with those given by the Takata-Ara test. Since the new test offers several advantages in simplicity and rapidity, I describe it here.

Method

Reagent	*Parts*
Chloranilic-acid solution 0·1% (*w/v*) ..	70·0
Sodium-chloride solution 0·85% (*w/v*) ..	5·0
Glacial acetic acid	0·2
Distilled water ad	100·0

The pH of this mixture is about 2·50. The reagent keeps almost indefinitely if stored in the ice-chest but deteriorates slowly at room-temperature and when exposed to light.

Procedure

To 2 ml. of the reagent in a small test-tube 0·1 ml. of serum is added, and the whole is mixed well. Precipitation usually takes place in a few minutes and is practically complete within 15–30 minutes. Readings can therefore be made after half an hour, but the precipitates must then be thrown down by centrifugation. Alternatively the samples may be left to stand overnight for sedimentation. Both these methods have been used and usually

give identical results. The following grading of the readings was used:

Precipitate	*Supernatant fluid*	*Grading*
Heavy	Clear	−
Heavy	Opalescent ..	(−)
Less heavy ..	Turbid	(+)
Small	Very turbid ..	+
Trace	Very turbid ..	++
None	Translucent ..	+++

Usually there is no difficulty in assessing the results, but occasionally it is not easy to decide whether a test is positive or not. In some very rare cases the reading after 30 minutes differs from that obtained after 24 hours. These cases include both normal sera which do not precipitate at once and pathological sera which give "false" precipitations on standing.

Since part of the chloranilic acid is precipitated with the protein, a more quantitative assessment may possibly be made by determining the amount of chloranilic acid (which is a dye) colorimetrically in the precipitate and/or in the centrifugate after treatment with trichloro-acetic acid.

Results and Discussion

For the selectivity of the test the pH of the reagent seems to be important. The influence of the pH (table I) was studied in the following way:

In 5 serum samples the test was made with the usual reagent (reagent 1). 3 of the tests were negative, 1 was read as +, and 1 as ++.

When a reagent was used which contained 1·0 ml. of glacial acetic acid instead of 0·2 ml. (reagent 4) +++ reactions were obtained in all the sera tested. The pH of this reagent was 2·44, and a pH of 2·86 was found in the mixture in the case of serum 1.

The substitution of 5 drops of 10% sodium carbonate for the glacial acetic acid (reagent 3) increased the pH of the reagent to 2·75, and of the mixtures of serum and reagent to 3·88 and 3·83; and the test, which had been positive in both sera, became negative. If the glacial acetic acid was omitted from the reagent (reagent 2), the change of pH in the reagent was only slight; it was larger in the mixture, and the test became decidedly less positive with serum 1.

As can be seen from table I, a relatively slight increase in pH of the reagent caused all the positive tests to become negative, whereas a decrease in pH had the opposite effect.

The possibility that the difference observed between normal and pathological sera was due to a difference in the final pH of the mixture was ruled out by measuring the pH in the centrifugates from tests made on 17 samples (table II). For comparison, in 13 of these cases readings with the Takata-Ara test are listed.

The pH in the 9 negative samples ranges from 2·93 to 3·19 (av. 3·07) and in the 8 positive ones from 2·96 to 3·09 (av. 3·04). The difference (if any) between the two series is clearly too small to be of any significance for the outcome of the reaction.

TABLE II—pH OF CENTRIFUGATES

Sample no.	Chloranilic-acid test		Takata-Ara test
	Reading	pH	
1	+	3·03	..
2	+	3·12	..
3	(+)	2·96	..
4	(−)	3·19	..
5	−	2·93	−
6	++	3·05	++(+)
7	+++	3·01	++(+)
8	(−)	3·01	−
9	−	2·94	−
10	−	3·08	−
11	−	3·09	−
12	−	3·16	−
13	−	3·11	−
14	−	3·12	−
15	+++	3·06	++
16	++	3·00	++
17	+	3·09	+

TABLE III—CORRELATION BETWEEN CHLORANILIC-ACID AND TAKATA-ARA TESTS IN 120 BLOOD SAMPLES FROM 25 * PATIENTS

Choranilic-acid tests		Takata-Ara tests								
		Negative (56)			Positive (64)					
		−	(−)	±	(+)	+	+ (+)	++	++ (+)	+++
Negative (67)	−	31	3	2	7	7	1	4	..	..
	(−)	1	3	1	1	1	..	..	1	..
	±	..	1	1	1	..	..	..	1	..
Positive (53)	(+)	4	2	2	3	8	1	3	1	..
	+	..	2	2	..	1	3	1	2	1
	+ (+)	1	..	..	..	3	5	..	..	..
	++	..	..	..	..	..	..	3	1	1
	++ (+)	..	..	..	..	..	..	..	..	..
	+++	..	..	..	..	..	..	..	1	2

Agreement was found in 86(83) samples (71·7(69·2) %).
Agreement was complete in 49 samples, good in 27(24) samples, and fairly good in 10 samples.
Discrepancy was found in 34(37) samples (28·3(30·8) %).
Positive Takata-Ara and negative chloranilic-acid test in 23(24).
Negative Takata-Ara and positive chloranilic-acid test in 11(13).
* Diagnoses: acute hepatitis (6 cases); hepatitis (2); hepatic cirrhosis (6 cases + 1 doubtul case of alcoholic cirrhosis); cholelithiasis (1); cholangitis or cholecystitis (?) (1); hepatic cyst (1); cancer of pancreas with metastases (1); heart-disease and icterus (1); leukæmia (1); sarcomatosis (1); mammary cancer (Op.), carcinomatosis (1); pulmonary tuberculosis (1); and proteinuria (1).

That the present test may be as useful as the Takata-Ara test in the diagnosis of severe liver damage is clearly shown by the excellent agreement between the results obtained by the two tests.

From Oct. 15, 1951, to Oct. 15, 1952, 650 blood samples were tested by both the chloranilic-acid and the Takata-Ara methods. In only 37 samples (5·8%) were dissimilar results obtained—i.e., the chloranilic-acid test gave 15 "false" positives and was negative in 21 samples which gave a positive Takata-Ara reaction.

All the 120 results recorded in the 25 patients from which the 37 samples mentioned were derived are shown in table III. They show that the two methods agree well on the whole but occasionally give discordant results, in some cases rather striking.

Since Jan. 15, 1953, the new method has been used as our routine method at the Aker Hospital, 1064 samples of blood being tested thereby up to Jan. 15, 1954. In 26 cases a Takata-Ara test was also made; in 3 of these cases a positive Takata-Ara was associated with a negative chloranilic-acid test.

The Takata-Ara test was usually made in cases where the clinicians threw doubt on the result of the chloranilic-acid test, especially where they thought that a negative result did not harmonise with the clinical picture. This may explain the higher degree of discrepancy (11·5%) between the two methods in this small series.

It may be inferred that the chloranilic-acid and Takata-Ara tests seem to be related in so far as they both reveal grosser changes in the proteins and thus may be regarded as approximate measures of the severity of the liver damage.

The test described here has, however, the advantage that it is much easier to make, because only a single tube is needed for each sample of blood, and the result can be obtained within half an hour if the mixture is centrifuged.

Summary

A new liver-function test (with chloranilic acid) is described.

The chloranilic-acid reagent gives voluminous precipitates in normal sera, whereas the precipitate formed in sera from cases of parenchymatous liver disease decreases with increasing severity of the liver damage. In the worst cases no precipitate is formed.

Like the Takata-Ara test the chloranilic-acid test detects grosser changes in the serum-proteins accompanying the more severe degrees of liver damage.

The test is easier and less laborious to make than the Takata-Ara test, and the result may be obtained within half an hour, provided the readings are made after centrifugation.

Preliminary Communication

SIGNIFICANCE OF ASCORBIC ACID IN THE ADRENAL CORTEX

THE significance of the high concentration of ascorbic acid in the adrenal glands, anterior pituitary, and corpus luteum is still obscure. Its rapid disappearance from the adrenals of animals exposed to various kinds of stress has not been satisfactorily explained, although the degree of depletion has been used for quantitative biological assay of adrenocorticotrophic activity.[1] The simultaneous reduction in the cholesterol content of the gland has led to the belief that both these substances are concerned with the production of the cortical hormones.[2] A second suggestion was that ascorbic acid might in some way be incorporated to render the steroid hormones water-soluble.[3] Vogt [4] and Oesterling and Long,[5] however, found no evidence to support either view. Recently, Dugal and Therien [6] have stated that though ascorbic acid fails to replace corticotrophin (A.C.T.H.) in maintaining adrenal weight in hypophysectomised rats, the two substances seem to act synergistically in this respect when given together.

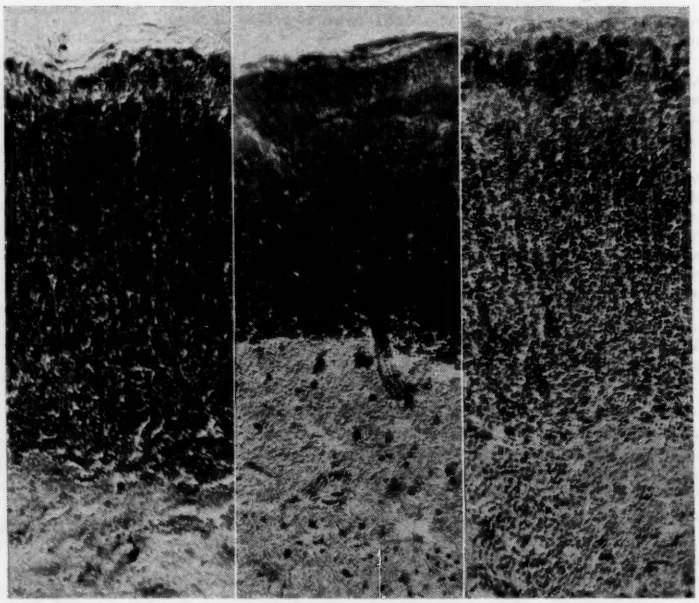
Hypophysectomy in the rat results within a few days in pronounced reduction of the adrenal weight.[7] Histological sections of such glands show atrophy of the zonæ fasciculata and reticulosa, owing to a great reduction in their cell volume. The consequent crowding of the nuclei in these layers becomes very conspicuous. Such atrophic glands also lose their high degree of sensitivity to corticotrophin as judged by Sayer's ascorbic-acid-depletion method. The administration of corticotrophin as replacement therapy can prevent this atrophy, and has in fact been used as an alternative method of assaying adrenocorticophic activity (adrenal maintenance test).

The possibility that the high concentration of ascorbic acid in the adrenal glands might have a rôle in maintaining the adrenal weight was investigated in the following experiment. Twenty male albino rats, each weighing about 100 g., were hypophysectomised and were divided into two equal groups. Each animal in the first group was given a daily intravenous injection of 100 mg. sodium ascorbate (Roche) in saline. Each animal in the second group was given the same volume of saline by intravenous injection. After a week all the animals were killed and their adrenals weighed immediately. A third group of ten intact animals of the same weight were also killed and their adrenals similarly weighed. The average weights of the glands in each of the three groups are shown in the accompanying table.

WEIGHTS OF FRESH ADRENAL GLANDS (MG. PER 100 G. BODY-WEIGHT)

Control rats	Hypophysectomised rats	
	Saline	Ascorbate
25·0 ± 1·2	12·2 ± 0·2	21·8 ± 1·3

These figures indicate that following hypophysectomy the reduction in adrenal weight, which would otherwise take place, can be almost averted by means of ascorbic acid only. The observed difference between the saline-treated group and the two others is statistically significant; that between the control and ascorbate groups is barely signifcant (P = 0·05).



a b c

Sections through adrenal cortex, fixed in formol saline and stained with Sudan III. (a) Intact control. (b) Hypophysectomised treated with saline. (c) Hypophysectomised treated with sodium ascorbate. (× 110.)

Frozen sections of such glands are shown in the accompanying figure. It appears that the adrenals of hypophysectomised rats treated with ascorbic acid contain much less cholesterol than the adrenals of the other two groups. Further work is in progress to find out whether ascorbic acid has any potentiating effect on the adrenal weight-increase or adrenal weight-maintenance produced by corticotrophin in hypophysectomised rats.

Department of Pathology,
Guy's Hospital Medical School,
London, S.E.1

H. H. KHALIL
M.B. Alexandria

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Medical Societies

ROYAL SOCIETY OF MEDICINE

Effects of Antibiotics

THE section of comparative medicine met on April 21, with Prof. T. J. BOSWORTH, the president, in the chair, to discuss the Effects of Antibiotics on the Host.

Prof. L. P. GARROD said that the ideal antibiotic would not harm the host at all; but of the many antibiotics which had been discovered only a very few had stood the test of time, because in one way or another they could be more harmful than beneficial to the host.

Five types of effect on the host could be recognised: toxicity, sensitisation, vitamin deprivation, super-infection, and growth promotion.

Toxicity.—Of all the antibiotics penicillin was by far the least toxic—astonishingly high concentrations of penicillin (even up to more than a thousand units per ml.) could be achieved in the blood without ill effect. One of the great dangers with streptomycin was the production of deafness, which might be permanent. The toxic effects of chloramphenicol on the bone-marrow had caused much discussion, and excessive doses of aureomycin and oxytetracycline (terramycin) were known to harm the liver. Polymyxin and bacitracin, particularly the latter, were apt to attack the kidney. Professor Garrod pointed out that his experience of these toxic effects was mainly in man. The effects in animals might be different; some effects in animals might also be more difficult to detect—for example, deafness in a cow.

Several antibiotics had been found to cause *sensitisation*. Some 20 cases of sudden death following administration of penicillin had been reported. These cases were thought to be anaphylactic; they apparently occurred always in persons who had had a previous injection, especially when procaine penicillin had been used. Penicillin and streptomycin were both commonly the cause of skin rashes, especially in nurses who were frequently handling the drugs, or when these antibiotics were applied repeatedly to the skin. Here again it was not so easy to say what happened in animals, in which some types of hypersensitivity reaction would be much more difficult to detect than in man.

Vitamin Deprivation after prolonged use of antibiotics had been described. This could be the result of suppressing the kinds of bacteria in the gut which contributed to the vitamin requirements of the host. Cases of this kind could not arise if vitamins were given with the antibiotic.

Super-infection was a serious problem and could take many forms. For example, a pneumococcal infection might respond to an antibiotic such as penicillin only to be replaced by a hæmophilus infection which failed to respond. The use of the "broad spectrum" antibiotics was sometimes followed by staphylococcal or candida infections of the air-passages or bowel: staphylococcal enteritis might be fatal. The mechanism of this type of catastrophe was at present obscure.

Growth Promotion.—This was one of the most interesting effects of antibiotics on the host. Professor Garrod would leave it to other speakers who were actively working in this fascinating field to say more about it.

Prof. ALAN KEKWICK discussed certain aspects of the pharmacology of penicillin, streptomycin, chloramphenicol, aureomycin, and oxytetracycline. Despite the very great volume of work that had been done, there were still enormous gaps in our knowledge of the optimum dosage of these drugs, in relation to route and frequency of administration, ease of absorption, excretion, toxicity, and so on. Often an adequate clinical response might be obtained with doses far lower than those customarily used; these usual doses sometimes approached the maximum which could be tolerated, though the tolerance might vary greatly between different species of animal.

Mr. W. S. GORDON, PH.D., after describing briefly the discovery of the growth-promoting effects of antibiotics, gave an account of the work which he and his colleagues have been doing in recent years in an attempt to find the mechanism responsible for this feature. Its occurrence was well established in many species of animals—including young children—and even in young plants as well. Increases in growth-rate of the order of 10–15% in treated over controls had been recorded, together with an improvement in food conversion, which resulted in more rapid fattening of pigs and poultry for human food with consequent increase in profit to the producer. Of equal, if not greater, importance, however, was the apparent reduction in clinical and subclinical infections which retarded growth.

Certain experiments gave a clue to the probable explanation. For example, the addition of antibiotics to the "germ-free" chick embryo did not stimulate growth, whereas after hatching a growth response could be elicited. The fundamental study of "germ-free" life by Professor Reyniers at the Lobund Institute of Nôtre Dame University clearly showed that "germ-free" animals derived no benefit from an antibiotic supplement, but would grow as fast as conventional, or bacteriologically contaminated, animals receiving such a supplement. The growth stimulation appeared to occur only in conditions where the environment had been contaminated by previous populations of the same species, and if the antibacterial properties of an antibiotic were removed it no longer appeared to possess the ability to stimulate growth. Even with concentrations of penicillin or aureomycin as low as 4 parts per million in the diet (approximately 0·13 mg. per kg. body-weight) antibiotic was detectable in the small intestine, stomach, and urine in the case of penicillin, and throughout the digestive tract with aureomycin. With concentrations of 128 parts per million in the diet (approximately 4·2 mg. per kg. body-weight), detectable levels in the serum were obtained with both antibiotics.

Mr. S. K. KON, D.SC., described experiments indicating that the effect of antibiotics on growth is related to environmental conditions. When a few years ago tests with antibiotics were begun at the National Institute for Research in Dairying, where chicks had been kept for a long time, positive results were consistently obtained; but workers at the Glaxo Laboratories found at the same time no response. Joint work showed that under otherwise identical conditions antibiotics were ineffective where chicks had not been kept before but improved growth in long-used premises. In these the antibiotics acted not so much by promoting growth as by removing a growth-depressing effect attributed to an inapparent "infection" in birds otherwise quite healthy by conventional standards. Further studies at the N.I.R.D. in isolation boxes showed that the "infection" could be transmitted by addition to the food of raw gut contents, but not of autoclaved ones of "infected" chicks or of those raw from "uninfected" birds. The gut weight of chicks responding to antibiotics was less than in the lighter controls. There was good indication that this effect on the gut was not direct but mediated by the microbial population since the gut-weight of "uninfected" chicks was not reduced by antibiotics. The nature of the "infection" was still obscure, and we had still much to learn both about the normal population of the gut of chicks and other animals and the effects on it of antibiotics.

Tonsils and Adenoids

The section of general practice met on April 21, with Dr. A. TALBOT ROGERS, the president, in the chair, to discuss the problem of Tonsils and Adenoids.

Dr. OLIVER PLOWRIGHT said that in children over 12–15 years old there was no problem: "If in doubt, take them out." The discussion was centred on younger children, and the two structures had to be considered independently. Sometimes the adenoids alone required operation, though not every surgeon could be persuaded of this. The indications for adenoidectomy were fairly straightforward; in the majority of cases there was either nasal obstruction, evinced by mouth-breathing with snoring in the absence of coryza, or recurrent otitis media or deafness. The mother's story, the child's breathing, and an indrawn fixed ear-drum on auriscopy usually led to the diagnosis. The indications for tonsillectomy were less universally agreed. Before the present century it was a rare operation; but recent surveys showed that at least a quarter of all children in England and Wales had been subjected to what the Medical Research Council termed "a routine prophylactic ritual" by the age of 14; and the proportion was higher in the United States. More than three-quarters of boys starting at Eton had had their tonsils out. Dr. Plowright thought that today repeated upper respiratory infections were commoner; in consequence tonsils were larger. Size was no index for operation, nor was persistent enlargement of the tonsillar lymph-gland; while chronic infection of the tonsil was difficult if not impossible to detect. He regarded the theory of focal sepsis as completely dead. Recurrent frequent tonsillitis with persistent lymph-glands, or one or two quinsies, pointed to the need for operation; but tonsillitis had to be distinguished from a plain sore throat, and recurrent colds suggested rather focusing attention on the adenoids, or better still on the conditions of overcrowding the child probably suffered at school and at home whence he drew his infections. The tonsils, after all, were there to protect the child, and should be preserved if possible. But it was often difficult to convince parents of this: unfortunately tonsillectomy had prestige in their eyes. Tonsillectomy was very rarely necessary for respiratory obstruction, or for treating the diphtheria carrier (when other methods had failed). A few children who had their tonsils and adenoids removed for no very good reason did proceed to grow and enjoy better health afterwards. But it was wise to be conservative: there were 85 deaths per annum from the operation; there were the psychological risks of night terrors and enuresis, to say nothing of sudden hæmorrhage or of the enhanced risk of bulbar paralysis in poliomyelitis.

Dr. WILFRID SHELDON agreed that tonsils and adenoids must be considered apart, and to Dr. Plowright's indications for adenoidectomy he added three diagnostic points. The first was that chronic sinus infection was commonly linked with enlarged adenoids. The second was that a child who was sick in the early mornings before breakfast, with a slimy vomit, had probably been swallowing mucopus all night, and needed attention to the adenoids; but neither of these associations was invariable and absolute. The third was a diagnostic warning. The child brought with a history of frequent absence from school because of colds, of much early morning sneezing, and of vigorous nose-blowing with very little result, was suffering from allergic rhinitis, for which operation on tonsils and adenoids was useless. Dr. Sheldon also advised caution in recommending tonsillectomy. Acute tonsillitis was a sign that the tonsil was functioning effectively as a trap for infection. Three attacks in a year meant nothing if the tonsils were healthy between them, and a source of infection in the household should rather be sought and treated. A tonsil was probably unhealthy, no matter its size, if there were congested vessels in the anterior faucial pillar, and if there were a granular pharynx and persistent firm lymphatic glands at the angle of the jaw and in the anterior triangle of the neck. A child who failed to thrive, or lost its appetite, might benefit from tonsillectomy, while some cases of vomiting and of bad breath were cured by this operation. He also believed that focal sepsis was still a valid idea; and tonsillectomy might relieve, for instance, recurrent nephritic hæmaturia. This operation was valuable in the treatment of tuberculous glands in the neck, because the tonsil was usually the portal of entry of the tuberculosis. Tonsillectomy should be done whenever tonsillar disease impaired the child's health, no matter what his age.

Mr. R. J. CANN explained that while the tonsil could be removed completely by dissection or by the guillotine (much more difficult—a dying art) because it had a capsule and was visible, the adenoids had no capsule, were more concealed, and had to be scraped away; so it was physically impossible to remove them completely. When the tonsils were completely removed, particularly in the first five years of life, lymphoid tissue around the pharynx tended to hypertrophy as a substitute for regeneration. Thus rounded mounds swelled up on each side of the tongue base (lingual tonsils); the pharyngeal wall became speckled with plaques of lymphoid tissue; and a thick band of it developed behind the soft palate, particularly around and in the eustachian openings, where it tended to cause persistent middle-ear obstruction and deafness. Further removal was extremely difficult, but radium or deep X-ray therapy could be used. This tendency to hypertrophy or regeneration was a further reason for conservation rather than operation. In the nasopharynx the size of the lymphoid tissue created the trouble; whereas in the fauces it was infection which called for the operation, though the number of attacks per annum was not the guide. He thought continuing deafness was commoner than recurrent otitis, and eustachian obstruction commoner than nasal obstruction, in bringing the patient to operation. Tonsillectomy was avoided during epidemics of poliomyelitis, not because it increased the risk of catching the infection, but because it enhanced the likelihood of the disease taking the fatal bulbar form.

The subsequent discussion showed general agreement on the necessity for operating on tonsils and adenoids independently, and for avoiding operation altogether whenever possible.

MANCHESTER MEDICAL SOCIETY

Asthma Treated by Oral Cortisone

AT a meeting of the section of medicine on April 7, Dr. WILLIAM BROCKBANK, with Dr. R. S. SAVIDGE, discussed the Treatment of Asthma with Oral Cortisone, on the basis of a blind trial on 24 patients severely incapacitated by asthma of long standing; their ages ranged from 17 to 70 years. 13 received regular maintenance doses of cortisone and 14 an indistinguishable control substance. 3 who were failures on the control were given cortisone. Of the 13 cortisone cases, 6 improved sufficiently to make a great difference in the ability to work and play; 4 more improved, but mostly subjectively; 1 was no better (this patient, who had severe emphysema, died eight months after the cortisone was discontinued); and 2 died while taking the drug. These results are very much better than in the control group; in 57% of this group there was no improvement, and 1 patient died. Side-effects of cortisone were few, increasing weight being the most important. The longest remission after withdrawal of the drug was eleven weeks. Most cases tended to relapse within a few days.

Cortisone cannot cure asthma, but some cases of long-standing chronic asthma can be effectively controlled by moderate doses of cortisone by mouth. But cortisone treatment is dangerous to life in some undefined types of asthma.

Reviews of Books

Peptic Ulcer

C. F. W. ILLINGWORTH, O.B.E., M.D., CH.M., F.R.C.S.E., F.R.F.P.S., regius professor of surgery, University of Glasgow. Edinburgh: E. & S. Livingstone. 1953. Pp. 287. 42s.

So much clinical and experimental research has been done on peptic ulcers that it is important from time to time to take stock of the facts and discard untenable hypotheses. Professor Illingworth does this with lucidity, simplicity, and elegance of language.

His own work on the incidence of ulcer in Glasgow enables him to condense the evidence as well as to indicate the fallacies in similar studies elsewhere and to emphasise the unexplained differences between peoples and places. In the section on gastric physiology he draws a clear distinction between speculation and fact that will be a great help to those who try to keep abreast of new work. The chapters on symptoms and treatment are outstanding, for here he writes with the intimate knowledge that only personal experience can give. The description and analysis of pain in peptic ulcer gives the reader a new comprehension of the experiences and reactions of an ulcer patient. Professor Illingworth's estimation of the value of the various methods of treatment, ranging from psychotherapy to surgery, is penetrating and practical.

The book is of modest size with well-selected graphs and illustrations and an extensive bibliography. It should be in the possession of everyone who deals with ulcer patients.

General Virology

S. E. LURIA, professor of bacteriology, University of Illinois. New York: John Wiley. London: Chapman & Hall. 1953. Pp. 427. 68s.

TEN years ago there were only one or two textbooks on viruses, but today nearly all self-respecting virologists have written or are writing one. Professor Luria's book is the first to treat virology as a separate branch of biology in its own right. His aim is to study plant, bacterial, and animal viruses as a group, despite uncertainty as to the extent of taxonomic kinship among what we call viruses.

He does not attempt to describe individual virus diseases or viruses; instead he deals with the facts and methods of virology as a whole. He first describes the techniques of virology and then the physical and chemical properties of virus particles in the resting state, and next considers virus-host interaction. Understandably, he gives most space to the bacterial viruses, since here the greatest advances have been made, many by himself and his colleagues. His experience with bacteriophages enables him to throw light on many important biological problems of animal and plant viruses, including variation, virus ecology, the relationship between viruses and tumours, and the origin and nature of viruses.

This book began as a course on viruses which Professor Luria gave to graduate and advanced undergraduate students at the University of Illinois. It has emerged as a collection of essays written with enthusiasm, imagination, and clarity, and it should appeal to mature as well as embryo virologists. Our respect for Professor Luria is only equalled by our respect for the intelligence of the students of the University of Illinois.

Medical and Scientific Investigations in the Christie Case

F. E. CAMPS, M.D., lecturer in forensic medicine, London Hospital Medical College. London: Medical Publications. 1953. Pp. 244. 30s.

FEW criminal cases have enough medical and scientific interest to justify the compilation of a book of this part of the evidence; but like R. *v.* Ruxton and R. *v.* Dobkin, the case of R. *v.* Christie was full of problems: it was a job for a team—the forensic pathologist, the microscopist, the toxicologist, the mycologist, the anatomist, and the dental histologist, with ancillary radiology, plan and diagram drawing, and photography, not to speak of the C.I.D., and counsel and psychiatrist for each side.

Notable contributions to this book come from Professor Miles on the dental identity studies and from Richard Harrison on the ageing, sexing, and stature estimations (for assigning skeletal remains to missing victims). The former give further encouragement to the use of Gustafson's method of "points-value" ageing of individual teeth. But the dental experts do not seem to have read Thomas Bell's *Anatomy, Physiology, and Disease of the Teeth* (1829) which described pink teeth accurately—nor Tomes's later copying of this account. Had they done so their "considerable speculation" would have been averted.

The anatomical work provides strong support for the recent American stature estimation tables of Trotter and Gleser—undoubtedly less inclined to overestimate than Karl Pearson's famous regression figures—and there are good colour diagrams for reconstruction data by Peter Cull which must have made the jury's problem much easier. American criminal courts are taking more readily to the artist than ours in England, and the Attorney-General's authoritative use of these colour plans is welcome.

Just as we despair of accuracy in estimating the lapse of time since death (and these studies provided no help in this respect) so we are beginning to learn more of the longevity, after death, of the sperm in the vagina, and of the consequent insecurity of opinion on the date of intercourse. Contrary to general belief HbCO and myo HbCO are also long-lived: more bench-work on this problem would have improved Smith's chapter on CO absorption.

This is a painstaking account of the enormous amount of work that forged the medical and scientific links in the chain of evidence against Christie. A vast amount of useful observation and well-informed reasoning has been piled into the text, which is well illustrated and produced.

Resection-Reconstruction of the Hip

Arthroplasty with an Acrylic Prosthesis. JEAN JUDET, ROBERT JUDET, JEAN LAGRANGE, JEAN DUNOYER. Editor: K. I. NISSEN. Edinburgh: E. & S. Livingstone. 1954. Pp. 151. 30s.

THE Judet arthroplasty, as it is usually called over here, achieved immediate popularity because of the simplicity and directness of its conception, the relative ease of its execution, and the excellence of its early results as compared with any previous form of hip arthroplasty. Large numbers of patients were subjected to the operation even though no-one knew what the late results would prove to be. Though the gloomier prognostications of early critics have not proved correct, complications have nevertheless been sufficiently numerous to provoke a smart reaction; and now some maintain that the operation should be reserved for elderly lightweights who are never going to put any great strain on the new joint.

The Judet brothers and their co-authors have done 850 of these operations, and they claim some 80% of excellent or good results in their more recent cases, in which they have used their new prosthesis; but they are at pains to emphasise that patients have to be selected with great care. The appearance of an English edition of their book will be welcome to all orthopædic surgeons in this country, and Mr. Nissen is to be congratulated on his editorship. The book is modestly written, and the difficulties and complications are described with an engaging frankness. Naturally, as the originators of the method, the Judets and their team have tried it in various conditions where there appeared reasonable hope of getting improvement—sometimes with disappointing results. Each type of disorder is discussed, and the chapter on late cases of congenital dislocation of the hip is particularly helpful, giving a clear picture of the limitations. The Judets use Hueter's approach as a routine, and believe that the exposure should be as limited as possible, so as to reduce interference with the blood-supply of the femoral neck. They obtained no better results with an extensive capsulectomy. In discussing the rationale of the operation in osteo-arthritis they say: "the femoral head is the principal site of pathological change, and hence the main source of pain"—a conclusion with which not all would agree. They now do an acetabuloplasty more often than not.

Their results, good and bad, are given with obvious fairness, and they do not attempt to put the method

forward as a panacea. They have been responsible for a great step forward in the surgery of the hip-joint, and much honour is due to them. This well-illustrated book gives a worthy account of their stewardship.

Man's Ancestry

A Primer of Human Phylogeny. W. C. OSMAN HILL, M.D., F.R.S.E., prosector, Zoological Society of London. London: Heinemann Medical Books. 1954. Pp. 194. 21*s.*

Dr. Osman Hill has converted a short course of lectures to Edinburgh students of social anthropology into an excellent account of the probable path of evolution from the lowest forms of life to man. Naturally, he gives considerable space to the emergence of the primates, the rise of the anthropoids (the Australopithecinæ are regarded as "essentially apes"), and the emergence of man. The various forms of fossil man and the chief prehistoric cultures, from palæolithic to iron-age, are briefly described. He concludes that man is not descended from an anthropoid ape but from some more primitive animal:

"The hominid line, after emerging from the common Eocene pool of tarsioids, must have been represented by an unspecialised quadrupedal monkey-like Primate, possibly represented by *Parapithecus*. The line leading to the apes separated from that which gave rise to Man probably in the Oligocene."

The illustrations are good and an abundant bibliography, a glossary, and an index round off a useful work.

French's Index of Differential Diagnosis

(7th ed.) Editor: ARTHUR H. DOUTHWAITE, M.D., F.R.C.P., senior physician, Guy's Hospital, London. Bristol: John Wright & Sons. 1954. Pp. 1058. 5 guineas.

THIS edition appears after a ten-year interval under the new editorship of Dr. A. H. Douthwaite, who has collected a strong team of contributors, mainly from the teaching staff of Guy's Hospital and the Westminster Hospital. He has had the help particularly of Sir Adolphe Abrahams, whose many articles are models for publications such as this.

Dr. Douthwaite would be the first to acknowledge the magnitude of the task he has set himself—to cover medicine, surgery, and obstetrics and gynæcology in one diagnostic volume.

Many of the articles are admirable—clear, brief, and to the point. Some others are less effective, perhaps because for some symptoms—notably the neurological—there must be long lists of causes and classifications, and differential diagnosis cannot be set out in a short article.

It must have taken much hard work and great determination to complete this book without excessive repetition or overlapping. The index alone, on which a main purpose of this book must depend, covers nearly 150 pages and is a comprehensive and successful achievement. There are over 700 illustrations, many in colour, and high praise must go to the publishers for the printing and production.

Doctors will find the new "French" a practical help in their daily work, and they should be grateful to Dr. Douthwaite and his colleagues for their careful, thorough, and skilled revision of an old friend.

Medical Terms

Their Origin and Construction. FRANGCON ROBERTS, M.A., M.D., F.F.R. London: Heinemann Medical Books. 1954. Pp. 88. 6*s.*

THE curtailment of a liberal education through too early specialisation, which is the usual lot of the modern medical student, has prompted Dr. Roberts to explain to those who lack knowledge of Greek and Latin how medical terms have been constructed and how new ones should be formed. As our correspondence columns have lately shown, this is a subject in which many would like enlightenment, and Dr. Roberts is always a lucid and lively expositor. But his book is designed on an elementary level, and it unfortunately contains a good many small errors which will alienate the kind of reader who already has any considerable knowledge of words and may be correspondingly sensitive to inaccuracy in their employment. Thus, though the word "eponyms" is used correctly, the word "eponymous" is used incorrectly to qualify the words instead of the persons who lend their names; "ballottement" is spelt wrongly; and the derivation of "anaphylaxis" is faulty, because Richet (who coined this word) preferred the meaningless "ana" as being more euphonious than the correct "a," meaning "without." Similar slips may be found every week in our own columns; but in a philological work they warn the reader that he is being addressed by a fellow doctor rather than a professional philologist.

Maxillo-Facial Laboratory Technique and Facial Prostheses

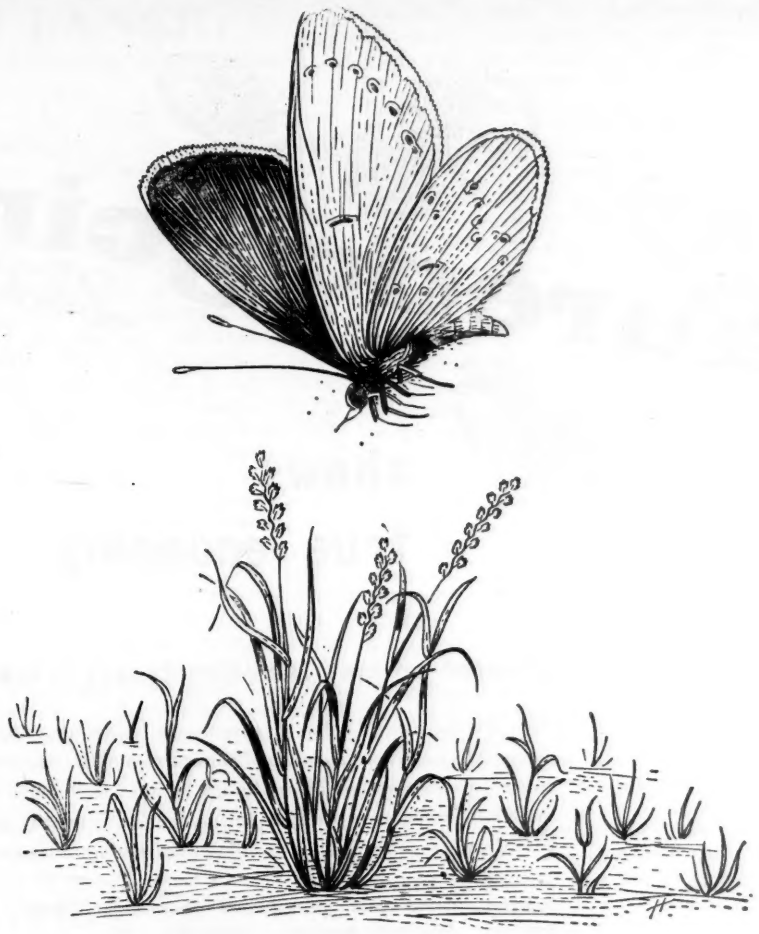
STANLEY BRASIER, chief technician, prosthetic laboratory, plastic surgery, burns, and jaw injury centre, St. Lawrence Hospital, Chepstow, Mon. London: Henry Kimpton. 1954. Pp. 230. 31*s.* 6*d.*

THIS is a good practical textbook for the trained dental technician who has no knowledge of the special procedures involved in making dental splints and non-dental prostheses. Plastic surgeons, too, may find it useful, for though in general they have not had enough technical training to be able to carry out the various laboratory techniques described, even if they wished to do so, they like to have a fair idea of what can be achieved with prostheses, as well as the limitations imposed by the materials available. There are a few statements with which both surgeons and dental surgeons may well disagree—e.g., "the edges of the ideal splint should extend into and beyond the gingival margin to a depth of about 2 mm." With all normal gingivæ this will rupture the peridental ligament. Again, if connecting bars between sections of a splint are situated only 1 mm. from the mucosa, as suggested, the maintenance of good oral hygiene will be much more difficult than if these bars have a clearance of 5–6 mm. Minor criticisms such as these do not really detract from the value of this book, which should certainly be in the possession of all technicians undertaking maxillofacial laboratory work.

Peripheral Nerve Injuries (2nd ed. Philadelphia and London: W. B. Saunders. 1953. Pp. 333. 35*s.*).—Dr. Webb Haymaker and Prof. Barnes Woodhall note in the preface to this edition that in the Korean conflict peripheral nerve injuries have presented many diagnostic problems to medical officers not familiar with them; and it is to such officers, as well as to medical students and civilian doctors, that their book is directed. The first edition lacked an account of the pathological changes in injured nerves, but this omission has now been made good in a new chapter; and there have been many other changes and additions in response to suggestions and criticisms. The numerous illustrations, too, have been augmented by a further 47, and greater emphasis has been given to pain, trick movements, contracture, and electromyographic studies. It is a useful work.

Medical Register (London: General Medical Council. 1954. Two volumes. 65*s.*).—This year the Register contains 83,090 names of doctors (a decrease of 824 since 1953). The new registrations in 1953 totalled 507 (2390 below the average for the last ten years). These figures are at first sight astounding, but they are explained by the fact that provisional registration has come into force and accounts for another 1813 persons who have passed all their qualifying examinations. The Commonwealth list of new registrations, which jumped from 471 in 1951 to 1452 in 1952, fell back to normal at 436 (plus another 50 on the provisional register); and the list of new registrations of foreigners shrank to 7 (average for the past ten years 295).

Simple Craft Jewellery (2nd ed. London: Faber & Faber. 1954. Pp. 69. 8*s.* 6*d.*).—Under the auspices of the Worshipful Company of Goldsmiths of London, Mr. Claude Geoffroy-Dechaume has been responsible for the introduction of jewellery-making into hospitals, as a form of occupational therapy. Since the first edition of this book appeared he has arranged special courses of training for occupational therapists all over the country, and many hospitals have introduced this enjoyable little craft to their patients. One London hospital has even established a small anodising plant to serve its own makers of jewellery and those in other hospitals. A film has been made showing how the work is done, which serves as a supplement to this pleasant and well-illustrated book.



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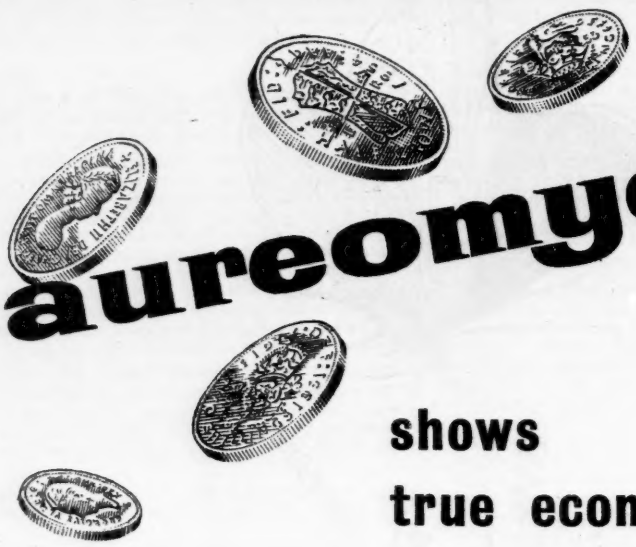

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LONDON: SATURDAY, MAY 1, 1954

Management of Coronary Thrombosis

In recent years preoccupation with the use of anticoagulants has perhaps tended to obscure other issues in the treatment of coronary thrombosis. WRIGHT et al.[1] and TULLOCH and GILCHRIST [2] have stated dogmatically that anticoagulants should be administered in all cases of cardiac infarction, and nearly all clinicians would agree that they should be given in cases of severe infarction accompanied by hypotension, circulatory insufficiency, prolonged pain, arrhythmia, or uræmia. Furthermore, anticoagulants may avert impending infarction in patients with progressively severe attacks of anginal pain occurring at rest as well as on effort.[3] On the other hand, there is a growing weight of opinion in favour of withholding anticoagulants from patients who have had a clinically mild infarction without prolonged pain, circulatory failure, arrhythmia, or much fever. RUSSEK and ZOHMAN [4] divided a group of cases untreated with anticoagulants into "good risks" and "bad risks," according to criteria similar to those already mentioned. The mortality was 60% in the "bad risk" group but only 1% in the "good risk" cases, while the incidence of thrombo-embolism was 10·6% in the former and only 0·8% in the latter group, although no anticoagulants had been given to either. LITTMANN[5] reported 112 "good risk" cases, not treated with anticoagulants, in which there were 5 deaths, none of which was found at necropsy to be due to thromboembolism. Pulmonary embolism occurred in 6 additional patients, of whom 4 were having anticoagulants and 2 were not. FELDMAN [6] found no difference in the mortality (30%) between 76 patients with myocardial infarction who had been treated with anticoagulants and 76 who had not. Although the difficulty of predicting which "good risk" cases will become "bad risks" within a few hours does suggest that anticoagulants should always be given, the risks and problems of anticoagulant therapy and the excellent immediate prognosis in most mild cases may persuade some physicians to restrict anticoagulant therapy to cases of severe infarction and to those with coronary insufficiency and threatened infarction.

The treatment of myocardial infarction does not begin and end with anticoagulants. Much remains to be learnt about the hæmodynamics and management of the acute phase in severe cases. CONNER and HOLT [7] and PARKINSON and BEDFORD [8] pointed out that in patients with shock and severe and continuing pain the immediate prognosis was grave, and sustained hypotension is clearly a source of danger. SELZER [9] found this complication in 69 of 528 unselected cases of myocardial infarction, and noted that the mortality-rate was more than double that of patients without shock. He divided hypotension in his cases into four categories: immediate and brief; immediate and irreversible; coinciding with, and apparently due to, cardiac arrhythmias; and delayed, associated with congestive failure, which was always fatal. Apparently two mechanisms are at work—peripheral vasomotor failure, and acute left ventricular failure—but whatever the contribution of each there can be little doubt that persistent hypotension, with resulting inadequacy of the coronary circulation, materially lessens the chances of recovery. Detailed hæmodynamic data in the acute stage would be of great value, but are very difficult to obtain. The physician, moreover, is in some difficulty in choosing therapy, being poised between the Scylla of overloading the heart by treating the peripheral failure with intravenous fluids, and the Charybdis of losing his patient as a result of prolonged hypotension. Accordingly the treatment in this stage has hitherto been based on the well-tried combination of morphine, oxygen, and intravenous aminophylline if signs of pulmonary congestion are present. Adrenaline is contra-indicated in view of its action in increasing cardiac irritability, and the danger of inducing ventricular fibrillation. More active treatment has been advocated. SCHWARTZ [10] and SAMPSON and SINGER [11] gave blood and plasma transfusions, without striking results. The use of pressor amines was suggested by BROFMAN et al.[12]; and *l*-noradrenaline, which does not increase cardiac output, and is said to increase coronary-artery flow,[13] has been given to relieve hypotension [14–16]: 4 mg. of *l*-noradrenaline bitartrate monohydrate ('Levophed') is dissolved in 1 litre of 5% glucose, and administered by slow intravenous drip at a rate that maintains the systolic blood-pressure at about 100 mm. Hg. SHIRLEY SMITH and GUZ [16] commented favourably on this method, while SAMPSON and ZIPSER [14] reported recovery of 20 out of 30 cases with severe hypotension in which *l*-noradrenaline was given. Although the value of this form of therapy has still to be proved, it seems well worth trying in cases with persistent hypotension, in which the prognosis is known to be very bad, despite the risk that it may cause serious arrhythmia. Digitalis, especially by the intravenous route, is held to be dangerous in view of the liability to ventricular fibrillation [17]; but if rapid auricular flutter or fibrillation develops, digitalis is essential to slow the ventricular rate.

When the patient is past the acute stage, further treatment consists in continuation of anticoagulants, bed rest, sedation, and a light, salt-free diet. The action of anticoagulants in preventing thrombosis in the calf and pelvic veins should be assisted by leg exercises, supervised if possible by a physiotherapist or nurse. Straining at stool should be avoided, and the bowels kept well open. The physical and mental stress associated with struggling upon a bedpan is more hazardous to the patient than the use of a bedside commode or transport to the lavatory on a portable

1. Wright, I. S., Beck, D. F., Marple, C. D. *Lancet*, Jan. 9, 1954, p. 92. See *Ibid*, 1953, ii, 171.
2. Tulloch, J. A., Gilchrist, A. R. *Brit. med. J.* 1950, ii, 965.
3. Wood, P. Diseases of the Heart and Circulation. London, 1950; p. 384.
4. Russek, H. I., Zohman, B. L. *Amer. Heart. J.* 1952, **43**, 871.
5. Littmann, D. *New Engl. J. Med.* 1952, **247**, 205.
6. Feldman, L. *Amer. Heart J.* 1952, **44**, 112.
7. Conner, L. A., Holt, E. *Ibid*, 1930, **5**, 705.
8. Parkinson, J., Bedford, D. E. *Lancet*, 1928, i, 4.
9. Selzer, A. *Amer. Heart J.* 1952, **44**, 1.
10. Schwartz, W. B. *Ibid*, 1947, **33**, 169.
11. Sampson, J. J., Singer, I. M. *Ibid*, 1949, **38**, 54.
12. Brofman, B. L., Hellerstein, H. K., Caskey, W. H. *J. Lab. clin. Med.* 1950, **36**, 802.
13. Goldenberg, M., Apgar, V., Deterling, R., Pines, K. L. *J. Amer. med. Ass.* 1949, **140**, 776.
14. Sampson, J. J., Zipser, A. *Circulation*, 1954, **9**, 38.
15. Miller, A. J., Baker, L. A. *Arch. intern. Med.* 1952, **89**, 591.
16. Smith, K. S., Guz, A. *Brit. med. J.* 1953, ii, 1341.
17. Travell, J., Gold, H., Modell, W. *Arch. intern. Med.* 1938, **61**, 184.

seat. Adequate sedation is important. LEVINE[18] has suggested that, once the acute phase is over, patients often do better if allowed to sit in a chair rather than lie in bed; he remarks on the reduction in bowel and bladder troubles, and the improvement in morale. Some support for this view comes from COE,[19] who measured the cardiac work in bed and in a chair, in 6 patients—3 without cardiac disease and 3 with degenerative heart-disease. In all 6 patients the cardiac work was appreciably less in the chair than in bed. The same is not necessarily true for patients who have recently sustained a severe infarction; and the "chair treatment," although widely used in America, has not become popular in this country. Complications such as congestive cardiac failure and arrhythmias will require treatment as they arise. Elderly patients tend to develop hypostatic infection at the bases of the lungs, and the signs of infection may be obscured by basal râles due to left ventricular failure and by the fever associated with the infarction; appropriate chemotherapy is thus of great importance. Many patients develop frequent ectopic beats, and these may be the precursor of auricular fibrillation, or, far more serious, of ventricular tachycardia. The incidence of these sequelæ may be reduced by the administration of prophylactic doses of quinidine (0·5–1 g. daily) or of procaine amide ('Pronestyl') (0·25 g. two to four times daily). In such doses these drugs have no hypotensive action, but in large dosage they may cause an undesirable fall in blood-pressure. After a major infarction patients should remain in bed for six weeks, after which six weeks' to three months' convalescence is usually needed. Every effort should be made to encourage the patient to return to as normal a life as is consistent with his cardiac condition, while avoiding undue sudden mental or physical stress.

The further prognosis is that of the ischæmic heart-disease, and is necessarily uncertain in the light of our present knowledge. That the outlook is not necessarily gloomy is shown by an analysis of 412 patients with myocardial infarction by MASTER and JAFFE,[20] who found that 40% recovered completely, and of these 83% returned to employment; only 3% died in under three years, while 40% survived for more than five years and 25% for more than ten years. COLE et al.[21] studied 285 patients who had their first infarction between 1932 and 1942 and who survived the first two months: 60% survived for more than five years, 40% for more than ten years, and 10% for more than fifteen years. These workers emphasise that the prognosis worsens with each succeeding infarct, and also that the longer a patient survives after one infarct the better is the immediate prognosis after subsequent infarcts, presumably because of the development of collateral vessels. Recent work points to disordered lipoid metabolism as the cause of atherosclerosis[22 23]; but there is still no incontrovertible evidence that any form of low-fat diet is of value in preventing further attacks of coronary thrombosis, despite the observations of Fullerton et al.[24] that fat ingestion influences coagulation. Moreover, Professor DUGUID, in his paper at the front of this issue, is somewhat sceptical of the relationship of coronary atherosclerosis (as opposed to simple fatty changes in the arteries) to disordered fat metabolism. Obesity, however, is known to exert a harmful influence in persons with degenerative cardiovascular disease,[25] and patients who are overweight should certainly be encouraged to reduce their weight.

While the uncertainties of prognosis must be made clear to the relatives, an attitude of optimism should be maintained towards the patient, who should be encouraged to regard himself, not as a hopeless invalid in fear of his life, but as a useful member of the community who, though obliged to live within the limits of his disability, can still earn his living.

18. Levine, S. A., Lown, B. *Trans. Ass. Amer. Phys.* 1951, **64**, 316.
19. Coe, W. S. *Ann. intern. med.* 1954, **40**, 42.
20. Master, A. M., Jaffe, H. L. *J. Amer. med. Ass.* 1951, **147**, 1721.
21. Cole, D. R., Singian, E. B., Katz, L. N. *Circulation*, 1954. **9**, 321.
22. Allen, E. V., Katz, L. N., Keys, A., Gofman, J. W. *Ibid*, 1952, **5**, 98.
23. Oliver, M. F., Boyd, G. S. *Brit. Heart J.* 1953, **15**, 387.
24. Fullerton, H. W., Davie, W. J., Anastasopoulos, G. *Brit. med. J.* 1953, ii, 250.

Malaria and Milk

IN the last two years several scattered observations on different aspects of malaria have been explained in the light of the discovery that a milk diet has an antimalarial effect. The story begins with work by MAEGRAITH et al.,[26 27] who were investigating what happened to *Plasmodium berghei* in rats if its supply of hæmoglobin were handicapped by feeding the animals on a diet poor in iron. For this purpose a milk diet was given, and it was found that the malaria parasite failed to develop. It was then found that the suppression of the malaria parasite had nothing to do with iron, but depended on some characteristic of milk. (Fresh cow's milk, dried cow's milk, and human milk were all effective.) This remarkable suppressive action of milk was confirmed in many different parts of the world and was shown to apply to other malaria parasites, such as *P. cynomolgi* and *P. knowlesi* in monkeys. The action was exerted only on the blood forms of the parasite and did not affect the pre-erythrocytic stages in the liver.[28]

The story entered a new stage when HAWKING[29 30] discovered that the suppressive action of milk was due to its deficiency in *p*-aminobenzoic acid, which was known to be a growth factor for many malaria parasites—especially *P. berghei* in rats and *P. knowlesi* in monkeys.[31] *p*-Aminobenzoic acid is well known as the bacterial growth factor which is antagonised by sulphonamides. The body-fluids of animals and man usually contain very little of this substance (otherwise sulphonamides would not cure streptococcal and other infections); but it is present in many diets, and when ingested in the food the blood-level rises sufficiently for malaria parasites to grow; it is rapidly excreted or destroyed, so constant renewal is necessary. Cow's or human milk usually contains extremely little *p*-aminobenzoic acid (only about 1 part in 200 million), which is insufficient for the growth of malaria parasites in either rats or monkeys; but if even 1 mg. is added daily to the milk diet of a rhesus monkey, infection with *P. knowlesi* can follow its usual acute and fatal course.

25. Master, A. M., Jaffe, H. L., Chesky, K. *J. Amer. med. Ass.* 1953, **153**, 1499.
26. Maegraith, B. G., Deegan, T., Jones, E. S. *Brit. med. J.* 1952, ii, 1382.
27. Liverpool School of Tropical Medicine, Annual Report 1952–53; p. 23.
28. Bray, R. S., Garnham, P. C. C. *Brit. med. J.* 1953, i, 1200.
29. Hawking, F. *Ibid*, p. 1201.
30. Hawking, F. *Ibid*, Feb. 20, 1954, p. 425.
31. Anfinsen, C. B., Geiman, Q. M., McKee, R. W., Ormsbee, R. A. Ball, E. G. *J. exp. Med.* 1946, **84**, 607.

Although a milk diet usually prevents infection of rats by *P. berghei* in a very striking manner, in certain animals this action is not manifested. Probably such rats contain in their intestine bacteria which can synthesise *p*-aminobenzoic acid and so maintain an appreciable level in the blood. Intestinal bacteria which synthesise many components of the vitamin-B complex are well known; but it is difficult to prove their presence except by procedures which themselves exert an antimalarial action. These exceptions to the antimalarial effect of a milk diet, although common in rats, have not been encountered in monkeys. The malaria parasite requires besides *p*-aminobenzoic acid many substances for growth—e.g., methionine and ascorbic acid. *p*-Aminobenzoic acid is outstanding because the parasite needs it but the host can flourish without it.

The recognition of *p*-aminobenzoic acid as a growth factor for malaria parasites explains many diverse observations. Thus it elucidates the antimalarial action of sulphonamides (since these antagonise *p*-aminobenzoic acid), and of proguanil and pyrimethamine which are known to be antagonists of folic acid (a complex derivative of *p*-aminobenzoic acid) and which resemble sulphonamides in many other ways. Secondly this observation links up with the extensive work of microbiologists in elucidating the rôle of *p*-aminobenzoic acid in cell metabolism. Briefly, in bacteria *p*-aminobenzoic acid is largely built up into folic acid or similar compounds; then these compounds (or perhaps the original acid) act as catalysts for various important synthetic reactions, including the formation of methionine from homocysteine and the synthesis of purine and pyrimidine rings. These substances are essential for the formation of nucleoprotein and so for the growth and multiplication of nuclei and cells. In the case of the malaria parasite there is morphological evidence for a relation between the supply of *p*-aminobenzoic acid and the division of the nucleus. By histochemical methods (e.g., Feulgen staining) it can be shown that the division of the parasite's nucleus to produce sixteen or more merozoites necessitates the formation of a great deal of new desoxyribonucleic acid. And it is just at this stage of the parasite's development that it succumbs and disintegrates under the antimalarial action of sulphonamides, proguanil, or pyrimethamine (each of which interferes with the use of *p*-aminobenzoic acid or folic acid).

Finally, these findings may have an important application to malaria in man. Although men and women rarely subsist on a milk diet, there is one important class of human beings who do—namely, babies. It has long been recognised that babies in regions of hyperendemic malaria do not contract the infection as early or as intensely as would be expected from the degree of their exposure to infected mosquitoes.[32] Hitherto it has usually been supposed that this insusceptibility was due to immunity transmitted in utero from the mother; but it now seems quite possible that the insusceptibility may rather be due to the milk diet. Suckling rats whose mothers have been placed on a diet free of *p*-aminobenzoate have proved relatively insusceptible to infection by *P. berghei*, but become highly susceptible if this compound is administered to them or to their mothers (thus increasing the concentration in the milk).[5] Similarly baby monkeys maintained on milk from the breast or from a bottle are insusceptible to infection by *P. cynomolgi*, but they readily become infected if they or their mothers are given *p*-aminobenzoate. The human parasites, *P. vivax* and *P. falciparum*, are sensitive to sulphonamides, so they presumably require *p*-aminobenzoate for their growth. It would be easy to jump to the conclusion that babies in West Africa are protected against malaria during the early months of life because they are fed exclusively on breast-milk, and that they become susceptible only when their diet is supplemented by foods containing *p*-aminobenzoate, or if the bacteria in their own or their mother's intestine synthesise this substance. But careful observation will be needed to prove such a hypothesis.

32. Bruce-Chwatt, L. J. *Ann. trop. Med. Parasit.* 1952, **46**, 173.

Epidemiology in Population Control

"GENERALLY, it is to be foreseene, that the Population of a Kingdome (especially if it be not mowen down by warrs) doe not exceed, the Stocke of the Kingdome, which should maintaine them." Thus, FRANCIS BACON anticipated the gloomy predictions of THOMAS MALTHUS. Ever since the publication of his essay, that English clergyman has been a centre of vituperative controversy.[1] Yet his basic postulates were indubitable: "First, that food is necessary to the existence of man. Secondly, that the passion between the sexes is necessary and will remain nearly in its present state." He then stated: "Population, when unchecked, increases in a geometrical ratio. Subsistence increases only in an arithmetical ratio. A slight acquaintance with numbers will show the immensity of the first power in comparison with the second." The happiness and welfare of a country depends on a balance between needs and material resources; with unchecked increases in population, "sickly seasons, epidemics, pestilence, and plague, advance in terrific array, and sweep off their thousands and ten thousands;" while "gigantic inevitable famine stalks in the rear, and with one mighty blow, levels the population with the food of the world." This "Malthusian scarecrow" has been dismissed by optimistic nutritionists, but ORDWAY[2] classifies such optimists as Cornucopians who believe that earth, sea, and atmosphere can deliver to the ingenuity of man an unending, inexhaustible supply of raw materials. Certainly the intensive development of agricultural methods in the past hundred and fifty years, which has allowed our planet to support a population of 2400 million, gives solid basis for that optimism. But as ORDWAY points out, in the United States in the past fifty years the population has doubled, while the consumption of minerals has increased eightfold and of fuel thirteenfold. There can be no comforting guarantee that the development of new material resources will keep pace with the pressure of needs. Conservation, he believes, is now the proper course; and in their recent discussion of public health as a demographic influence, Prof. JOHN GORDON and his colleagues[3] share this cautious approach. Stung, no doubt, by VOGT's acid comment that physicians have "set the stage for disaster, and like PILATE, wash their hands of the consequences"

1. Smith, K. The Malthusian Controversy. London, 1951.
2. Ordway, S. H. Resources and the American Dream: a Theory of the Limit of Growth. New York, 1953.
3. Gordon, J. E., Wyon, J. B., Ingalls, T. H. *Amer. J. Med. Sci.* 1954, **227**, 326.

(a thought which EVANG,[4] as a doctor, has expressed in less astringent terms), they review the repercussions of public-health practice in furthering population increase and suggest ways and means for harmonising population size and food-supply.

Realistic appraisal is the first task of epidemiology—the diagnostic science of public health. If population pressure be regarded as a disease of a society, an epidemiological survey of present circumstances will show its geographical distribution. In fact, the Asian peoples present the most serious economic and public-health problem. Western curative and preventive medicine has increased the population potential by cutting death-rates in circumstances of high fertility. In India, for example, between 1921 and 1941, declining mortality allowed a population increase of 83 million. As long as present birth-rates continue, population increases will tend to outstrip food production, leaving a precarious balance between needs and resources. Emigration and colonisation of undeveloped territory has long been the result of such pressure; but we are now approaching the limits of territorial expansion and overcrowding. Where that alternative is not available, the results of population increase can be disastrous. In British Guiana, for example, an effective antimalarial campaign between 1945 and 1948 reduced the infant-mortality rate from 250 per 1000 to 67 per 1000, with the result that by 1948 only 1500 calories per head were available to the people of the country. In India the caloric intake per head fell from 1976 to 1570 between 1934 and 1951. Where, as in Japan, an island community has no outlet for expansion, the problem is particularly acute. Ireland, Puerto Rico, and Sicily exemplify the drive towards emigration fostered by failure to achieve a satisfactory ecological balance between food and mouths. Only the Western nations of the U.S.A., United Kingdom, Scandinavia, and France have attained a reasonable stability in population numbers. The reasons for these disparities between countries in their demographic trends may suggest useful courses of action. The success of measures to control mortality depends on the whole population acquiescing in their application. The control of fertility must likewise depend more on general measures than on the unconcerted action of individuals. Such measures must take into account the historical and cultural background of a nation. A long period of high mortality demands a compensatory high level of fertility; and even when the death-rate falls, national procreative habits persist. Religious scruples determine both the drive towards family limitation and the methods used. Again, methods designed for adoption throughout a country must be both practicable and widely acceptable. While drugs such as phosphorylated hesperidine may prevent the sperm entering the ovum, it is unlikely that many men or women could be persuaded to achieve continual sterility by taking a tablet three times a day every day of life. GORDON and his colleagues believe that the traditional methods of epidemiology must be applied. The first essential is to recognise impending ecological disequilibrium from a simultaneous rise in population numbers, fall in the average available number of calories per person, rise in unemployment, and increase in political ferment. Measurement of severity is the second essential for intelligent control; this calls for a detailed analysis of fecundity and fertility and their relation to marital habits and population age structure. Finally a carefully planned and controlled field trial will be needed to assess the efficacy of any measure of population control designed for universal use in an overcrowded community. Only thus, GORDON believes, can we fulfil COBBETT's recipe for rural content—that "the labourer must have his belly full and be free from fear."

In all this GORDON and his associates betray a caution which is hardly typical of their country. "Americans," said Mr. ADLAI STEVENSON, "have always assumed subconsciously that *all* problems can be solved, that every story has a happy ending"; and a report from the Rockefeller Foundation and the Twentieth Century Fund [5] certainly suggests that there is a technical answer to every problem of human population needs. Yet CROMWELL would have approved of GORDON's tempering blind faith with an informed caution in order to maintain man's control over his own ecological balance.

4. Evang, G. *Eugen. Rev.* 1953, **45**, 247. See *Lancet*, March 13, 1954, p. 558.

Annotations

SPREAD OF MYXOMATOSIS

LAST October myxomatosis appeared in Kent, and since then it has been recognised in some eighteen areas, mostly on the South Coast but extending north to East Suffolk. We still do not know how the disease reached us from France, and there is no apparent connection between the various epidemic foci here. Official attempts to limit the area of infection by rabbit-proof wire fencing were, as we said,[6] almost certain to fail; and the report [7] of an advisory committee of the Ministry of Agriculture shows that this policy was rapidly abandoned. Faced with the probability of widespread myxomatosis in which 90% of the country's 100 million wild rabbits may perish in the next two years the committee has tried to forecast the economic consequences of such an epizootic. The total income from the wild-rabbit meat and fur trades is about £15 million. This is roughly the same as the damage caused by rabbits to cereal crops alone; and when we add to this the damage to pasture, vegetable crops, and young trees and the cost of pest protection, then the loss caused by the depredations of rabbits is likely to be three or four times as much. Nine rabbits are said to eat as much as two sheep; and in South-East Australia, where four-fifths of the rabbits were killed by the disease, the increase in rural production was estimated at £50 million. There is already evidence, however, that in some areas of Australia the mortality-rate from myxomatosis has fallen considerably; and if, as seems likely, this continues the gains may be short-lived.

While nothing can usefully be done to arrest the natural spread of myxomatosis in wild rabbits in this country, the protection of tame rabbits is important—among other reasons, because some 40,000 are used every year for diagnostic and research work. The only known prophylactic is a preparation of the living virus of Shope's fibroma, and this is now being studied at Weybridge. Some workers in France claim that this

5. Woytinsky, W. S., Woytinsky, E. S. World Population and Production: Trends and Outlook. New York, 1953.
6. *Lancet*, 1953, ii, 1031.
7. Report of the Advisory Committee on Myxomatosis, Ministry of Agriculture and Fisheries. H.M. Stationery Office, 1954. 9*d*.

vaccine has not come up to expectations, and clearly we need much more information. Meanwhile breeders should take all possible precautions against the introduction of infection, and mosquito-proof screening and insecticides must be used until we know how the disease is spread. At present we rely on the excellent Australian work to guide us about the epidemiology of the disease, but this may have little relevance to conditions here. The introduction of myxomatosis into this country provides the epidemiologist and ecologist with a unique opportunity not only to provide practical information but to study what may be, in effect, a field experiment on an enormous scale.

A YEAR'S WORK IN THE TROPICS

THE report for 1952 of the Institute for Medical Research at Kuala Lumpur [1] describes an impressive amount of work.

'Daraprim' (pyrimethamine) gave a disappointing cure-rate in the treatment of malaria caused by *Plasmodium falciparum*. There were 13 failures in 97 cases of acute infection; increasing the total dose to 0·3 g. in five days did not improve the rate and produced leucocytopenia. Proguanil in doses of 400 mg. daily for a week failed to cure most attacks due to *P. falciparum*. Laboratory workers are glad to hear that the small Malayan *Macacus irus* monkey can act as a reservoir of *P. knowlesi*. Some of these monkeys have been imported to European laboratories to restock with fresh strains the dwindling strains maintained in rhesus monkeys.

American workers based on Kuala Lumpur have completed their stay and have now described interesting observations on rickettsial immunology. Clinical scrub-typhus has a latent period of about ten days and burns itself out naturally within two weeks of infection. Smadel and his colleagues [2] have isolated *Rickettsia tsutsugamushi* from an axillary lymph-node fifteen months after a natural infection. Using chloramphenicol to control the disease, they inoculated volunteers intradermally with known doses of the Karp strain, and demonstrated that immunity to a homologous strain lasts several years but infection with a heterologous strain is possible within a few weeks of the initial infection.[3] By starting to administer chloramphenicol on the seventh day after inoculation they produced in volunteers both a demonstrable rickettsæmia and a long-lasting immunity (shown by subsequent challenge doses) with little or no overt clinical typhus.[4] This production of immunity by chemoprophylactic control of a pathogenic vaccine in vivo is of some theoretical interest; but as Smadel et al. point out, it is of limited practical value because of the difficulty of exact dosage and timing of vaccine and prophylaxis. In 1941 a similar procedure [5] was tried in South Africa, when sulphonamide was given to subdue infections in cattle with the rickettsia of heartwater disease.

Filariologists in Malaya add some interesting findings on treatment of *Wuchereria malayi* with diethylcarbamazine ('Hetrazan'). Some physicians have stopped using this drug on account of the sharp febrile reaction and allergic skin manifestations to which it quickly gives rise. The reaction is thought to be due to the release of parasite protein after the death of the microfilaria, and anti-histamine drugs do not entirely eliminate it. The severity of the reaction does not necessarily depend on the number of circulating microfilariæ, and the workers in Malaya now report that it seems to be independent of the size of the initial dose. They also point out that once this reaction has subsided the dose can be increased up to fourfold without ill effect. They have given one dose daily, which they find adequate. Reappearance of the microfilaria in the blood is slow, taking place over a year or so. (It is commonly believed that hetrazan kills the microfilaria and damages the production of it without actually killing the adult worm.) Nevertheless the decimated microfilaræmia has the effect of controlling transmission through mosquitoes. When the 1st Battalion Fijian Regiment left Fiji all those whose blood showed *W. bancrofti* were treated with hetrazan: on arrival in Malaya only 43 out of 725 had microfilaræmia, and in these the numbers were very low. A similar epidemiological situation arises with the arrival of East African troops infected with *Shistosoma hæmatobium*, and the entomologists are busy finding out whether this can be transmitted by any local fauna.

1. Federation of Malaya: Annual Report of the Institute for Medical Research, 1952.
2. Smadel, J. E., Ley, H. L. jun., Diercks, F. H., Cameron, J. A. P. *Amer. J. Hyg.* 1952, **56**, 294.
3. Smadel, J. E., Ley, H. L. jun., Diercks, F. H., Paterson, P. Y., Wisseman, C. L. jun., Traub, R. *Amer. J. trop. Med. Hyg.* 1952, **1**, 87.
4. Ley, H. L. jun., Diercks, F. H., Paterson, P. Y., Smadel, J. E., Wisseman, C. L. jun., Traub, R. *Amer. J. Hyg.* 1952, **56**, 303.
5. Neitz, W. O., Alexander, R. A. *J. S. Afr. vet. med. Ass.* 1941, **12**, 103.

RENAL FAILURE COMPLICATING PEPTIC ULCER THERAPY

ALKALOSIS and renal dysfunction due to excessive intake of milk and absorbable alkali in the treatment of peptic ulcer was first described by Hardt and Rivers [1] over thirty years ago. Cope [2] reviewed the condition in 1936 and emphasised the importance of hypercalcæmia from high calcium intake. A patient who has had this treatment for many years begins to complain of weakness and lethargy with impaired mental efficiency and powers of concentration. This may progress to stupor or even to terminal uræmic coma. The urine, often increased in volume to three litres or more daily, is alkaline in reaction and usually contains small quantities of albumin and hyaline or granular casts. The levels of blood-urea and of bicarbonate, pH, and calcium in the serum are all increased.

The disorder was further defined by Burnett et al.[3] in 1949, and Dufault and Tobias [4] have now described four further cases. The patients in order to alleviate ulcer pain often insist on taking vast amounts of milk —in some cases a gallon daily. (In a striking example recorded by McQueen [5] this almost amounted to an addiction, the patient continuing to take milk despite the warnings of his physician.) This amount of milk contains 5·6 g. of calcium, which is many times the calcium content of an ordinary diet. Some patients take considerable quantities of calcium carbonate as well. If renal function is normal, excess dietary calcium is excreted in the urine and significant hypercalcæmia does not develop.[6] This hypercalcuria in a constantly alkaline urine leads to the progressive deposition of calcium phosphate in the distal and collecting tubules and eventually to renal failure and uræmia. At this stage the calcium output cannot be maintained and there is increase of serum calcium and phosphate, often leading to widespread metastatic calcification. Corneal calcification is of especial diagnostic importance; it is readily recognised in early cases by use of the slit-lamp and later by naked-eye examination.

It has been shown that the intake over short periods of large quantities of alkali and milk does not impair renal function.[7] In most of the reported cases a high intake has been continued for many years before renal failure developed. This may develop more rapidly if there is unrelated renal disease, or after temporary acute

1. Hardt, L., Rivers, A. *Arch. intern. Med.* 1923, **31**, 171.
2. Cope, C. L. *Clin. Sci.* 1936, **2**, 287.
3. Burnett, C., Commons, R. R., Albright, F., Howard, J. E. *New Engl. J. Med.* 1949, **240**, 787.
4. Dufault, F., Tobias, G. J. *Amer. J. Med.* 1954, **16**, 231.
5. McQueen, E. G. *Lancet*, 1952, ii, 67.
6. Knapp, E. L. *J. clin. Invest.* 1947, **26**, 182.
7. Van Goidsenhoven, G. M. T., Gray, O. V., Price, A. V., Sanderson, P. H. Communication to Medical Research Society, December, 1953.

renal failure associated with severe hæmatemesis or pyloric stenosis. Rapidly developing uræmia secondary to hypercalcæmia is known to occur in many other conditions, particularly hyperparathyroidism,[8] multiple myelomatosis,[9] calciferol intoxication,[10] and sarcoidosis.[11]

The early diagnosis of uræmia associated with hypercalcæmia is of paramount importance since the renal failure is potentially reversible. Determination of the serum-calcium is essential since reliance on the Sulkowitch reaction for hypercalcuria may be misleading when excess calcium is no longer being excreted. The avoidance of alkalis together with a low calcium diet may be all that is required in treatment, but in severe cases the use of calcium-chelating agents, particularly ethylene diamine tetra-acetic acid, may be of great value initially.[12] This compound does not reduce the serum-calcium level but converts a portion to a biologically inactive complex which is excreted more rapidly. Differential diagnosis may be difficult in a comatose patient incapable of giving a history. The hypercalcæmia of excessive milk intake and of calciferol intoxication will respond to conservative methods alone; that associated with some cases of myelomatosis and sarcoidosis has been shown to be corrected by corticotrophin or cortisone.[13 14] Hyperparathyroidism will prove resistant to all measures other than surgical removal of the causative adenoma.

GRADUATE WIVES

EDUCATION is an expensive but enduring possession, and in their latest broadsheet[15] P.E.P. consider whether we are making the best possible use of married women graduates. Each year 4000 women graduate from our universities, and in due course about three-quarters of them marry. What happens to them? During the years when they are bringing up their family their education—as distinct from any vocational training—is certainly being well used. But are we giving them the opportunity to use it in middle age by returning to work suitable to their qualifications? P.E.P. have looked at these questions against the background of facts supplied by a survey of married women graduates made by Mrs. Judith Hubback, M.A.

Mrs. Hubback's findings are based on the answers to a questionary sent out, in 1953, to 2000 married women who had taken their degree in and after 1930 at Oxford, Cambridge, London, Birmingham, Durham, Reading, Nottingham, the University College of Hull, the University of Wales, St. Andrews, and Aberdeen; and 1165 (58%) of them replied. An almost identical set of questions was answered by 420 married women of the same age-group, none of whom had been to a university: they were drawn from the sisters, relatives, and friends of those who filled in the first set of questions.

Of the graduates, only 1% said they would not, if they had their lives over again, go to a university at all; and almost three-quarters said that they would study the same subject or subjects over again. Of the non-graduates, only 52% were satisfied with the education they had received, and would do the same again. Just under two-thirds of the graduates, and a comparable proportion of the non-graduates, had planned a career for themselves (other than marriage), though the careers aimed at by the two groups were slightly different. In both groups, however, teaching was a common choice: 34% of the graduates and 14% of the non-graduates had planned to teach.

Marriage ended the planned career more often among non-graduates than graduates; and a larger proportion of non-graduates (79%, as against 64% of graduates) found housework to be a full-time occupation. The size of the families was much the same in the two groups, and both experienced much the same difficulty in getting domestic help. About half the women in each group enjoyed domesticity, and the rest either tolerated it or regarded it with mixed feelings. About 19% of the graduates and 9% of the non-graduates were doing paid full-time jobs, and 34% of the graduates and 11% of the non-graduates were doing part-time paid work. Many women seek work when their children are old enough to spare them. Of the 1165 women graduates questioned, nearly 500 plan to work at some chosen job in the future and a further 88 intend to do some work but have not yet decided what sort.

In summarising these findings the broadsheet does less than justice to the contribution made to the community by women graduates—"it is probably fair to say that the majority of the graduate wives covered by this sample were making no direct use of their academic qualifications"—for in fact more than half of them were doing full-time or part-time paid work likely to draw on their education. But the return we expect from education in this country cannot be assessed entirely in terms of paid work, and, as the broadsheet points out, "the indirect contribution which a trained mind and cultured outlook can make to family life and to the life of the nation generally is very great indeed." Education is never wasted, and least of all on those who have the task of civilising the next generation.

BRACKEN POISONING

BRACKEN poisoning occurs in horses and cattle, and it can be produced experimentally in sheep and rats. In horses the condition is known as "bracken staggers," since incoördination is a prominent sign. "Bracken staggers" is a manifestation of thiamine deficiency, caused by a thiaminase contained in bracken, and the condition can be cured by administration of thiamine.[1] In ruminant animals the signs of bracken poisoning are different.[2] Sheep or cattle receiving a diet that contains more than 40% of bracken may continue to thrive for some weeks. Then the animals lose appetite, have a raised body-temperature, pass blood with the fæces, which become soft and contain much mucus, and die within a few days. The disorder is not improved by thiamine injected or given by mouth; and it seems that bracken poisoning in such animals, unlike that in horses or rats, is not associated with thiamine deficiency. The level of pyruvate in the blood of affected animals increases little, and the level of thiamine in the tissues is only slightly reduced.[3]

Naftalin and Cushnie[4] have described their hæmatological and necropsy findings in adult cattle and young calves that had died after being given bracken. The essential lesion is extensive bone-marrow damage, affecting the megakaryocytes, the primitive white cells, and the primitive red cells; thrombocytopenia and leucopenia result. Subsequently there are multiple hæmorrhages, and bacterial invasion of the blood-stream leads to a generalised non-specific bacteræmia. After the onset of bacteræmia hæmorrhage becomes more severe and leads to death. Though erythropoiesis is affected, the number of circulating red blood-cells is little reduced until the onset of severe hæmorrhage. Moon and McKeand[5] have reported the hæmatological changes in sheep given bracken. Poisoning is indicated by a progressive fall in red cells and hæmoglobin, though leucopenia and thrombocytopenia are also found. The

8. Albright, F., Baird, P. C., Cope, O., Bloomberg, E. *Amer. J. med. Sci.* 1934, **187**, 49.
9. Limarzi, L. R. *Med. Clin. N. Amer.* 1951, **35**, 189.
10. Adams, F. D. *New Engl. J. Med.* 1951, **244**, 590.
11. Longcope, W. T., Freiman, D. G. *Medicine, Baltimore*, 1952, **31**, 1.
12. Spencer, H., Vankinscot, V., Lewin, I., Laszlo, D. *J. clin. Invest.* 1952, **31**, 1023.
13. Thorn, G. W., Forsham, P. H., Frawley, T. F., Hill, S. R., Roche, M., Staehelin, D., Wilson, D. L. *New Engl. J. Med.* 1950, **242**, 824.
14. Phillips, R. W. *Ibid*, 1953, **248**, 934.
15. *Planning*, 20, no. 361, April 5, 1954. Obtainable from P.E.P. (Political and Economic Planning), 16, Queen Anne's Gate, London, S.W.1.

1. See *Lancet*, 1952, i, 140.
2. Stockman, S. *J. comp. Path.* 1917, **30**, 311. Moon, F. E., Raafat, M. A. *Ibid*, 1951, **61**, 88.
3. Moon, F. E., Raafat, M. A. *J. Sci. Fd Agric.* 1951, **2**, 228.
4. Naftalin, J. M., Cushnie, G. H. *J. comp. Path.* 1954, **64**, 54, 75.
5. Moon, F. E., McKeand, J. M. *Brit. vet. J.* 1953, **109**, 321.

difference from the blood picture in bracken-fed cattle may be due to the ability of sheep to tolerate bracken feeding for much longer periods. Red cells have an appreciably longer life than white cells, and probably cattle do not survive long enough for the changes in the bone-marrow to affect the red-cell count. Several groups of earlier workers [6] reported similar hæmatological changes in cattle with bracken poisoning, but the cause of the bone-marrow lesions in ruminants is not yet known.

The ruminant differs from simple-stomached animals in that it depends for its nutrition largely on the metabolic activity of the micro-organisms in its rumen. These micro-organisms break down cellulosic material, assimilate nitrogen from the feed, and synthesise vitamins of the B complex and vitamin K. When the mixture of food particles and micro-organisms passes from the rumen into the abomasum, or true stomach, the bacterial cells are broken down and their contents become available for absorption through the normal digestive processes. Bracken poisoning in the ruminant may result from disturbance of normal microbial activity in the rumen leading to a deficiency in the animal of some nutrient necessary for the maintenance of normal bone-marrow function. Several groups of workers [3–5] have excluded the possibility of this nutrient being one of the known vitamins of the B complex, vitamin K, or vitamin C; but, as Naftalin and Cushnie point out, the dysfunction may be caused by lack of some essential amino-acid or of some still unidentified vitamin. An alternative hypothesis is that bracken contains a factor (or causes the rumen organisms to produce one) with a toxic action on the bone-marrow. But so far the only noxious principle discovered in bracken is thiaminase, which probably plays no important part in the production of bracken poisoning in ruminants.

VECTORCARDIOGRAPHY

THE diagnostic reliability of the electrocardiogram is now so soundly established that it is easy to forget that the absolute limits of normal—particularly of the P–R interval, and of the width of the Q R S and the Q R S T complexes—are still not exactly agreed. Variations due to age, posture, and perhaps race, in addition to those caused by instrumental distortion, faulty technique, and inaccurate measurement, constitute the chief difficulties in the way of establishing statistically acceptable criteria.[7] The use of newer leads, although invaluable in diagnosis, has increased the problem. There are other theoretical objections to the present electrocardiogram: the standard and unipolar limb leads and the chest leads record electrical activity only in the frontal plane of the body, although the heart, being a three-dimensional structure in a volume conductor, has electrical forces in other planes. The study of these forces as spatial vectors was first undertaken by Mann in 1920 but made little progress because their determination from successive measurements of the electrocardiogram was tedious even when aided by optical devices, such as that of Shillingford and Brigden.[8]

The conception, put forward by Wilson and his colleagues,[9] of the ventricular gradient has helped both in understanding the electrocardiogram and in distinguishing changes in the T wave due to abnormalities of Q R S from those due to local abnormalities of the myocardium. The gradient is a vectorial expression of the combined electrical forces producing the Q R S and T waves. Its magnitude is calculated by planimetry from the algebraic sum of the areas bounded by the Q R S and T deflections and its direction determined by plotting measurements in any two standard leads on Einthoven's triangle or Bayley's triaxial reference system. Fundamentally it is a measure of the duration and magnitude of the electrical forces produced by lack of uniformity in the processes of excitation and repolarisation of the heart muscle. Ashman and his associates [10] have worked out normal values for the ventricular gradient and have found them to vary within wide limits; but they have been able to establish constant spatial relationships between the direction of the gradient, the Q R S vector, and the long anatomical axis of the heart, and have shown that the gradient lies posteriorly to the long axis and the Q R S vector still farther behind. Unfortunately measurement of the ventricular gradient is difficult and too cumbersome to be really useful in practice.

The adaptation of the cathode-ray oscilloscope by Shellong and others in Germany, and by Wilson and Johnston,[11] has made it possible to record automatically the time-course of the cardiac vectors. In some ways the direct vectorcardiograph is a more sensitive instrument for studying the myocardium than the electrocardiograph, but it has considerable limitations—for example, in the study of temporal relationships such as the P–R, Q–T, and T–P intervals—while normal standards are hard to define. In addition, a standard reference frame has still to be agreed on. Some favour Wilson's equilateral tetrahedron with the Einthoven leads and Wilson's central terminal, recording in the frontal plane, supplemented in the sagittal plane by an electrode on the back; whereas others prefer more complicated frames, such as those proposed by Duchosal and other Continental workers. The Wilson frame is at least simple in practice and has the theoretical advantage of being based on the Einthoven triangle. The presentation of frontal and sagittal loops so that they can be viewed as a single spatial vectorcardiogram is not easy. Stereovectorcardiograms have been attempted in several ways, including double photography of model loops and the use of additional electrodes to define other planes, but they are unsatisfactory in practice. A special circuit with unequal resistances producing oblique-plane vectorcardiograms which can be viewed simultaneously on adjacent oscilloscopes has been devised by Burch et al.,[12] and seems more promising. In an attempt to overcome the spatial limitations of frontal-plane leads, Trethewie [13] has proposed an interesting simplified electrocardiography. By placing an electrode on the manubriosternal junction and another at the xiphisternum, with two others at the same horizontal level in the left midaxillary line and at the back of the right chest near the midline of the back, he has been able to record three leads at right-angles to each other. These should detect electrical abnormalities of the heart in both horizontal and vertical directions of the frontal plane as well as in the sagittal plane. Satisfactory electrocardiograms have been obtained from cases of known heart-disease, but confirmation from larger numbers is needed. Variations in the normal values of the leads, especially of the T wave in the horizontal lead, require statistical study if the method is to be of more than theoretical interest.

It is unlikely that either vectorcardiography, which is still chiefly a research method, or Trethewie's simplified system will replace electrocardiography. In doubtful cases clinicians, probably rightly, rely on the case-history and on other methods of examination rather than on statistical criteria.

6. Schofield, F. W. *Rep. Ont. vet. Coll.* 1947, p. 127. Guilhorn, J., Julou, J. *Bull. Acad. vét. Fr.* 1949, **22**, 407; *Ibid*, 1950, **23**, 185. Evans, E. T. R., Evans, W. C., Hughes, L. E. *Vet. Rec.* 1951, **63**, 444.
7. Kossman, C. E. *Circulation*, 1953, **8**, 920.
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11. Wilson, F. N., Johnston, F. D. *Ibid*, 1938, **16**, 14.
12. Burch, G. E., Abitoskov, J. A., Cronvich, M. S. Spatial Vectorcardiography. New Orleans, 1953.
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Special Articles

TREATMENT OF THE CHRONIC MENTAL PATIENT

J. A. R. BICKFORD
M.R.C.S., D.P.M.

CONSULTANT PSYCHIATRIST AND DEPUTY PHYSICIAN-SUPERINTENDENT, DE LA POLE HOSPITAL, WILLERBY, YORKS

IF a layman were to visit the nearest mental hospital he would see patients who had been admitted ten, twenty, fifty years ago; and he would wonder at the poverty of the resources at the command of psychiatry, that these fellow citizens should have existed for so many years in such a state and yet be as far from being cured as they were on the day of their admission.

In the De la Pole Hospital there are some 450 men other than those in the admission ward and the convalescent ward, and 67 of these have been in the hospital for less than one year. The remainder have been in for periods shown below:

Duration of Stay (in years) of 384 Patients

	2–4	5–9	10–14	15–19	20–24	25–29	30–39	over 40
Number ..	63	87	46	63	37	38	29	21

Psychiatrists are no less intelligent than general physicians; and mental nurses are probably more efficient, and certainly much more humane, than nurses in other kinds of hospitals. Mental hospitals are ugly and uncomfortable, but so are many other general hospitals. Why should results be so bad?

There are many points to be considered. Each doctor in a mental hospital will have under his care hundreds instead of tens of patients. The total cost of a mental patient is not likely to be more than £5 a week, whereas the cost of a general patient will be usually more than £10, and of a sanitorium patient, or a patient in a maternity hospital, it will be nearer £12–15 a week. Out of this money, the sum set aside for medical care for each patient will be some £2 in a general hospital; in a mental hospital it is about 4*s*.

The patient who develops a mental illness would be shocked if he knew how little the community is prepared to spend on him. If he asked about it, he might be told that he would be fed and sheltered and all his physical needs would be looked after; but that once his nursing was paid for there would be hardly any money left to pay for medical attention. There is in fact a general if unspoken belief that the patient in a mental hospital has no need of a doctor, and that he must be glad to be kept alive. Even the procedure of being kept alive is not perfect; perhaps for tens of years he will go without touching solid food after 5 P.M. He will usually be clad in shapeless tweeds, sometimes many years older than himself. Often he will be unable to go out of doors because he will have no shoes. As he eats, so will he sleep and live—without any privacy, and often in the company of 50–100 others. Such fresh air as he gets will be in a courtyard about twice the size of a tennis-court, surrounded by high railings. He may well feel that he matters little to his fellows.

The psychiatrist who works in a mental hospital has to contend with all these conditions; yet it can be truly said that he fails to make the most of his opportunities. The sickness from which psychiatry suffers is fundamentally that of the whole community: things are always divided into opposites, the good and the bad, the quick and the dead, the sheep and the goats; and to these categories doctors (and psychiatrists in particular) add the acute and the chronic, the curable and the incurable.

All psychiatrists agree that no effort must be spared to cure the patient when he first falls sick. So he is admitted to a modern, well-furnished, and comfortable ward; he is treated sympathetically and energetically, and conferences are held by the medical staff to ensure that he is treated by the most effective means available. If he fails to recover within some three to six months, his treatment changes; he is still treated with kindness and sympathy, but skill and energy are tacitly withdrawn. He becomes a chronic patient; and as the tempo of his illness changes so does that of his treatment. He is moved from the admission ward to the main building where he is kept physically healthy. Spontaneous remissions of his mental illness are often observed (though the mode of his care discourages their occurrence); yet when they do occur they are not always acted upon. The statutory documents are accurately and regularly completed during the tens of years which remain. Where will he live, and how will he live?

There will be no privacy, no curtains or carpets, no pictures on the walls—save possibly framed illustrations from the Christmas magazines of the last century. Some two or three times a year he will see his doctor; if he particularly requests it he will get special interviews, but they will all be short: he is very lucky if he has any form of medical care directly from his doctor for more than half an hour in each year. His doctor cannot help this: he has many other patients. If the doctor works in both the admission wards and the chronic wards he will spend half his time in the one, seeing some 30 patients, and the remaining half in the other looking after some 200 patients. Or he may spend his whole time looking after the 30 patients in the admission ward, while his unfortunate colleague will spend his whole time looking after 400–500 patients in the chronic wards.

Clearly the psychiatrist feels that the acute patient needs more of his very limited time than does the chronic patient. Is this contention true? I suggest that it is absolutely untrue. In the admission wards patients with acute illnesses treated by physical methods get better or fail to improve almost independently of any psychotherapy they are given. Those psychiatrists who work in the admission wards are those who dictate the policy of the hospital, and the admission wards are well favoured with doctors—to such an extent, indeed, that the patients are overburdened with medical attention. The psychiatrist no less than the patient appreciates the pleasant furniture and surroundings of the admission ward; it is agreeable to talk to patients who are well dressed and who can talk sensibly. The senior psychiatrist will not willingly surrender these pleasant things to work in the æsthetically unpleasing and culturally barren atmosphere of the chronic wards. In the admission wards he is always surrounded by a relatively large proportion of patients who are improving—patients who remit spontaneously, and patients who cannot help but get better on physical treatments. But between the admission wards and the chronic wards there is a gulf bridged only by the chronic patient.

The Chronic Patient

The facile distinction into "curable" and "incurable" patients is not confined to the administrative buildings of a hospital but is spread far around. Sometimes the hospital has a block of buildings for acute, recent, and eminently recoverable patients some miles away from the buildings used for the chronic patients. Sometimes a city will have a hospital or two for acute cases; patients who do not respond rapidly to treatment in these hospitals are discharged, and have to seek admission to another hospital which rarely admits cases of good prognosis. In it are usually found cases of organic intellectual deterioration, epilepsy, recurrent and chronic psychosis, and mental defect. Everywhere there are more doctors in the small hospitals than in the large overcrowded hospitals for chronic patients.

The rational treatment of psychotic illnesses is impossible unless their natural history is known; but very few psychiatrists have any conception of the natural course of these diseases. Schizophrenia will eventually remit: perhaps not for ten, perhaps not for fifty, years; but remit it will. The parole wards of mental hospitals are full of patients who have reached their remissions. They may still have some odd ideas, but they have learnt to live normally, and to avoid talking about their strange experiences or reacting to them. The possession of delusions is no reason why any patient should remain in hospital: what counts is the effect of the delusions on his behaviour. Patients with paranoid illnesses can be taught to live with their delusions unchanged but with their attitude so much modified that they need not be in hospital. Pathologically quarrelsome and difficult epileptics are often admitted to mental hospitals; but if they are handled with tact, kindly discipline, and encouragement they can be made fit to go home and live with their relations. The restless and violent senile patient rarely remains in this state for more than a week or two; after that he can easily be looked after, and the first step is to arrange for his admission to a geriatric unit.

Incarceration for the sake of incarceration is, of course, unknown; but spontaneous remission and adaptation are only rarely given an opportunity to develop. Yet praiseworthy efforts are made to make life in hospital pleasant for the chronic patient: occupational therapy classes, social clubs, frequent entertainments, games to watch and play, outside excursions in the summer, and instruction in painting and sculpture are all encouraged to some extent. These activities sound very impressive, and are ennobled by the name of "therapy"; but a visit to any occupational class will show this description to be false. The pattern is always the same: patients do, and continue to do, what they have some gift for doing. Patients make rugs who have done nothing else for years; women knit who would knit wherever they were: they would knit if the heavens were falling and the world crashing down around them. Painting is done by patients who have a gift for painting. There is nothing therapeutic in the overwhelming majority of occupational classes up and down the country. Occupational therapy has become an end in itself, the teachers and the taught indulge in activity which from the point of view of treatment is quite meaningless and absolutely useless.

Fitting Patients for Discharge

Psychiatrists who deal with chronic cases forget that the urgent need is to get patients out of hospital fit to work while they still have relations who are willing and able to look after them. The adolescent who develops an acute schizophrenic illness may remit in his late fifties; but by then he is unlikely to have fit and active parents, or even siblings, with a strong enough affection to look after him.

It should be made clear to patients when they enter hospital that they will not be allowed to stay indefinitely. The patient who leaves the admission ward for the chronic wards must be made to understand that his treatment has not finished, but rather that it has taken on the more obviously purposeful form of getting him fit to return to his home and work. A patient's relations will probably remain loyal to him and be prepared to look after him, even if he is not completely well, provided he is discharged within a year of his admission to hospital. If ten years have elapsed he may be completely well and yet be unable to leave hospital because he has no-one to befriend him.

The wards of a chronic hospital often contain 80–100 patients, and it is instructive to see how these patients pass their day. In the report book it may be stated that all but ten of them are working, either in or out of the ward. In fact, some dozen patients will be out of the ward from 10 A.M. to NOON, and from 2 to 4 P.M.; 8 will go to occupational therapy classes, leaving 60–100 patients to clean and maintain the ward: and how they can all be usefully employed defeats reason. There are, in each ward, as many beds and chairs as there are patients; there are sufficient tables and a few leather sofas; there are lavatories, washbasins, and 4 baths; and there is the ward crockery. Surely it cannot take 60 or more patients all day to keep these objects tidy and clean—even though the curious importance attached to a well-polished floor consumes uselessly a considerable amount of time and labour. A patient is counted as "doing ward-work" if he carries a chair from one place to another at the direction of a nurse. No ward of this size could possibly take up the time and labour of more than a dozen patients, even if they took things very easily.

How then goes the rest of the day for the 60 patients who remain in the ward? They sit, or walk aimlessly about the airing-court or the ward; and do nothing else. Sometimes they are seen sitting tightly on benches against which a table has been pushed, because there seemed to be no other way of preventing them from fighting one another.

The annual reports of mental hospitals rightly stress the good work that is done, the new methods of treatment employed, the increasing number of cures, the provision of better recreational facilities and so on. Encouraging as it is to read these reports it would be even more encouraging if the hospital were to state the problems which have still to be solved and state them unmistakably in figures: reporting, for instance, how many patients have been kept in bed for disciplinary reasons; how many times disablement resettlement officers of the Ministry of Labour have failed to find work for patients who were fit for discharge; how many patients could not be discharged because there was no home for them to go to; how many were incontinent habitually; how many times the procedure for the follow-up of discharged patients has been inadequate, and how often this has led to the death of ex-patients.

An Experiment

In this hospital we are happy in that there has been for many years a liberal régime. Villas and open wards are available for about a third of the male patients; every day there is some form of entertainment; and parole outside the hospital grounds, as well as within, is readily granted. Despite these and many other good points the problem of the so-called dilapidated chronic patient has not been touched.

A patients' sports and social club did some good: an elderly man with an active delusional system, a most difficult patient, was transformed by this opportunity, and his good work for the club became well-known and widely appreciated throughout the hospital. He was willingly granted outside parole, and remains in hospital for no other reason than the lack of a home outside. An epileptic of poor intelligence, who for many years had been rightly regarded as one of the most dangerously aggressive patients responded to the same opportunities so well that he was granted first inside, then outside, parole and at last became a voluntary patient. When he left hospital he attended an industrial rehabilitation unit and was selected for a job.

Despite these measures the wards and their airing-courts were as full as ever of dilapidated patients, many of them regarded as actively homicidal and suicidal, many known to be incorrigible escapers for whom no control seemed effective except the one so readily adopted—confinement to the ward and all too often to bed.

The male side of the hospital was chosen for an experiment. The aim, it was agreed, should be to discharge all these apparently helpless patients in such a state that they would be fit to take and hold a job,

and live satisfactorily in lodgings or with their relations. Before a patient could be considered fit to do these things he must have proved himself fit to live in the hospital in a parole ward and to work in the hospital free from supervision.

The chronic wards were told to choose 6–12 patients for their hour-to-hour maintenance. Patients who worked usefully about the hospital or its grounds continued to do so. Every other patient was to be out of the ward in the morning and the afternoon. Apart from its dozen essential workers, then, each ward was emptied every morning and afternoon, and the patients were divided into groups, according to their age and physical fitness, and in these groups they worked or played. The fact that a patient was regarded as a persistent escaper, a homicidal or suicidal risk was taken as an absolute indication that he should be kept out of the wards and included in one or other of the groups.

Patients who were young and fit did what was essentially physical training, combined with games requiring thought. (Football, which tends to be purely mechanical pursuit, was forbidden except as a weekly game.) These patients trained together as a large group until they had learnt to do things as a well-coördinated unit; then they were divided into smaller groups wearing distinctive sports gear, so that each rank in the large unit was made up of different small groups. After a further period, each group worked on its own, always under the same nurse. Patients had to do things smartly and do them as a group. They were given things to do which they would enjoy doing, and which would provide them with thought as well as physical exercise, and everything they did had to have their active and their willing support. As they were seen to improve, individuals were put on a gardening squad, first under the care of a nurse and later under a gardener, and eventually they were given other jobs about the hospital or its grounds with the least possible supervision.

Older patients would sit about in the grounds, throw a light medicine-ball to one another, gather cut grass, or play cricket with a soft ball, never taking any strenuous exercise, or doing anything for so long that they became bored or physically overtired. They were encouraged to play bowls. Blind and infirm patients also left the wards and sat about or walked according to their physical abilities or their wishes.

There were some 20 patients who had all been in the hospital for many years and for whom no activity had ever been thought possible. Their behaviour was constantly violent and uncoöperative, and they suffered almost continuously from distressing hallucinations.

They were placed under the care of one nurse and given a large plot of rough ground. It was explained to the nurse that this ground belonged to the patients, and that it was his responsibility to turn it into a couple of tennis-courts, a bowling-green, and an ornamental garden. He was told that he could take as many years to do this as he found necessary, and that he would never be given any patients who were likely to be helpful or coöperative. The ground was rough, the grass stood high, and it was rank with stinging nettles and docks. His men were given forks and spades but no other equipment. The details of the work were left to him, and he was told he would be given no assistance or advice by the hospital gardeners. The work has gone well, the grass was burnt or torn up, the turf has been cut and stacked, the ground is being prepared. The Hospital Management Committee allow the patients to buy seed potatoes from them, and they buy back the crop; the patients will have the profits to buy fresh equipment.

The patients on this project, specially picked because they were difficult and uncoöperative, work very well and enjoy it. They resent wet days when they cannot go to their tasks. Once classed as "impossible" and "untrustworthy," they never make any attempt to run away, and they require only minimal supervision.

Nor is all this extravagant of nursing staff. No patients have been left in the wards except those whose behaviour was very good; and their numbers were few so that ward nurses could readily be spared. Complete disuse of the airing-courts also released nurses; and in fact it was found that 180 patients could be well looked after by 8–10 nurses.

The whole of these activities were placed under the care of the hospital's good occupational therapy department. It was held that no patient should go to the occupational therapy department just because he was no trouble and worked well there. Patients can deteriorate as rapidly making rugs as they can while working with the hospital porters or just sitting in the wards doing nothing. We decided there must be a positive reason why they should indulge in any form of activity. The advantage of having the occupational therapist in charge of all these activities was that each separate activity remained a part of the whole and there were no separate kingdoms claiming allegiance from patients or demanding the allocation of additional nurses. A patient could easily be transferred from one unit to another as his progress dictated, still remaining under the same set of nurses.

On wet days, patients might give a ward an unusually good cleaning; and the recreational hall was used for some of the same sorts of activities as were carried on out of doors. With the coming of winter there had to be a change, though the improvement in the patients rather than the difference in the weather made it necessary. Other treatments were introduced. Young and active patients still continued to take physical exercise when possible, but in bad weather they were divided into groups of 12 who, with a nurse in charge, would sit and discuss the news of the day, read to one another, discuss their previous careers, or the places they had visited, read or write plays, listen to school broadcasts and discuss them, and so on. A group of deteriorated schizophrenics gave a very creditable concert. In the morning and afternoon the old men used one of the dayrooms in a villa as clubroom. Patients with gross organic brain damage, or a severe degree of mental deficiency, were given the job of constructing a cinder-path round the grounds, which will be useful to everybody because it is free from traffic. The emphasis, in this as in all other labouring activities, was on the therapeutic value to the patient of being employed usefully, and seeing that his work will benefit him and his fellows. No patient is kept at one job all the time; other ways of occupying him are introduced. The important thing is that the patient should see what he is doing and enjoy it; and no attempt is made to get the job finished in a given time.

Every effort is made to get patients home for the day, or the weekend, as soon as they show any sign of improvement. If there are no willing relatives, a nurse will take two or three patients into the city for an afternoon, and when a patient—who may not have been out of the hospital for twenty years—has improved enough, and gained enough confidence, he is encouraged to go on his own. If relations are willing to have him home but are not convinced that he is well enough, a nurse will accompany him on the first occasion.

We accept that view that all psychoses have an organic cause; and the usual physical methods are used where they are indicated. A doctor who looks after 400–500 patients can give psychotherapy only at a superficial level, but it is an essential adjunct to other methods of treatment. It is important for the patient to be able to accept his false beliefs and his disabilities, and yet to be able to refrain from acting upon them: for the habit of acting on them usually makes it impossible for him to live out in the community.

Every request a patient makes for a change of ward or for leave is carefully considered, and the fact that he has behaved badly in the past is not allowed to weigh

too heavily against him—indeed the historical approach to a patient is discouraged. The patient who was dangerous twenty years ago is only too apt to be still classified as a desperate homicidal risk.

When a patient is transferred to the main building from the admission ward, the reason for this is explained to him. He is told that the plan is to get him discharged soon, and every effort is made to win his coöperation. I have said that a patient does not have to be free from delusions to be fit to leave hospital; nor need his conduct necessarily be perfect under all circumstances: whose is? A patient whose behaviour is impossible in one ward may behave perfectly in a parole ward, and be fit in every way to visit the city on his own, to seek work, obtain it and keep his situation.

Results

That this régime is successful needs no elaboration: the testimony of surprised and delighted relations and the great decrease in the amount of sedative drugs dispensed confirm this fact.

In the sick ward for older deteriorated patients, whose strength has declined with the years, many beds may be occupied by people who could, if they were encouraged, get up to go to the toilet, to eat, and to go out of doors when the weather permits. These patients tend to lie in bed, taking no interest in anything, constantly incontinent, and running a risk of developing contractures. In this hospital these patients are up and dressed and given simple occupational therapy—making paper bags for the canteen, sorting wool, and making rugs. Some who were formerly thought to be completely demented, and a permanent burden on the nurse, have become cheerful, more alert, and able in small ways to look after themselves and to get some enjoyment out of life and out of their families' visits. Within six months of starting this experiment there was not a male patient who was not receiving some form of active treatment every weekday.

Our revolution has been achieved without any increase in staff, without any patient being deprived of treatment which he needed because nurses were engaged with other tasks, and without the purchase of expensive equipment. Indeed it has been carried out without a penny's cost to the hospital. Confinement to bed is unnecessary, seclusion should never be employed, and it is rarely necessary to lock wards. Locked wards on the male side of this hospital are decreasing in number, and soon two-thirds of the male chronic patients will be in open wards. It is my belief that locked wards will eventually be dispensed with in all hospitals.

When the patient leaves hospital he will have to work; and he is therefore encouraged to work while he is in it. Meaningless tasks, such as hospital portering, are discouraged, and patients should never be allowed to continue doing them for more than a few weeks at a time without some pleasant and therapeutic activity being introduced as a break. A recoverable schizophrenic is not uncommonly discovered on the swill gang or on some other similar job where he will hardly ever see a doctor. Patients must have it explained to them time after time that they will one day leave hospital, and that they must prove themselves fit to start work and to lead a normal life by the time that day arrives.

Some Future Possibilities

If the opportunities were provided for patients to receive some pay for work when their stay was likely to be more than a few weeks, there are few who would not be fit to work and glad to do so. The problem of providing work for discharged patients could easily be solved, if industry would coöperate. Epileptics and chronic psychotics would be employed in a separate workshop, where they would not distress others by fits or strange behaviour.

Many patients require somewhere to live on first leaving hospital: a hostel run by nurses and supervised by the hospital would be of great service to them. Moreover, patients who have been in hospital for a long time often find it impossible to get work. Their relations might be willing to have them at home if they were occupied; but the prospect of having them about the house all day and every day makes many refuse to have them at all. We arrange that discharged patients can attend at the hospital on all weekdays for occupational therapy, and have their midday meal there. They are allowed one day off, to attend at the labour exchange to look for work themselves. The same device is used for treating those not needing inpatient care, but requiring supervision and help.

For the success of such a plan as ours one thing is necessary: the willing coöperation of the nursing staff. Once this is gained much becomes possible.

Conclusion

Though psychiatrists and nurses are kind and humane people, treatment for any but recent admissions is generally almost non-existent in mental hospitals. Psychotics have an almost irresistible tendency to recover; but the process is checked because most psychiatrists are unaware of the natural course of psychotic illnesses. Moreover, the community is united in refusing to accept the psychotic when he has recovered from his illness even if he is an efficient and willing worker.

The psychiatrist can always be sure of the help of his nurses if he proposes to put into action a plan such as that described here. There are nurses everywhere—just as there are here—who will volunteer to look after a group of apparently irredeemable and degraded patients, and will eventually help these fellow citizens to regain a life which is pleasant and useful not only to themselves, but to their relations and to the community.

CANCER RESEARCH

THE 51st annual report of the Imperial Cancer Research Fund shows that its policy has not yet succumbed to the view [1] that cancer research should devote itself to chemotherapy and that the cancer problem can be solved only by retreating to basic sciences like genetics and biochemistry.

At the Fund's laboratories, L. M. Franks and P. C. Williams have studied the relation of œstrogens to prostatic cancer, using the hamster and guineapig for their experiments. It is now well known that a considerable proportion of old men show histological evidence of symptomless prostatic cancer and benign enlargement of the gland. Changes resembling human nodular hyperplasia or adenocarcinoma have only recently been reproduced in experimental animals: firstly, adenocarcinomas have been obtained by subcutaneous transplants of mouse prostate, together with hydrocarbon-carcinogens; and, secondly, local application of "the carcinogen" (presumably œstrogen) to ageing œstrogen-treated hamsters has induced acinar carcinoma of the prostate resembling that seen in man.

Williams has observed the effect of cross-breeding a strain (RIII) of mouse liable to mammary cancer with the C_{57} strain which has shown no tumours during six years' observation at the Funds' laboratories. The C_{57} line shows a high vaginal responsiveness to œstrogen and there appears to be an inverse relation between œstrogen sensitivity and incidence of mammary cancer. The hybrids (C_{57} x RIII) show a higher incidence of mammary cancer than even the C_3H line, and their vaginal œstrogenic sensitivity is nearly as great as that

1. Committee on Growth of the National Research Council: 6th Annual Report to American Cancer Society. July, 1950, to June, 1951. 1953.

of the C_{57} mice. The comment of the report is a little hard to understand: "The assumption of a causal significance is not supported by tests carried out on the Foulds hybrids (C_{57} x RIII)." (It may be that the theorists cannot bear to have their generalisations upset.)

The theme of the day in cancer research—the lung-cancer/smoking relation—is being pursued by A. M. Begg. A single intranasal inoculation of benzpyrene in arachis oil induces oat-cell carcinoma in Simpson mice after 200 days. The report mysteriously adds that "Dr. Begg has also been carrying out tests in rats, mice and rabbits of substances which, because of their nature and use, must necessarily be subjected to adequate tests for absence of carcinogenic activity."

C. Le Q. Darcel and G. Negroni are investigating fowl leucosis by tests on the transmissibility of lymphomatosis and erythroblastosis, the viral transmission factors, and the cytology of the tumours. Because one type of tumour is transmitted by cell-free extracts, and therefore by a viral-type agent, while the other is not, analogy between the two diseases suggests that a viral factor cannot be excluded in the second case, but that it could be too labile or liberated in too small amount to be demonstrated by the techniques so far developed.

"Claims have been made by other workers to have demonstrated that cell-free extracts produce these tumours after a long latent period, but they also found that extracts of normal chick embryos have a similar activity. The active agents in these extracts therefore cannot be analogous to the erythroblastosis virus of the fowl since the virus can only be obtained from homologous tumours and not from normal tissues of apparently normal fowls."

James Craigie's technique of preserving tumour tissue has had some remarkable results: primary benzpyrene sarcomas, induced in C_3H mice, could still be grafted successfully after five years' storage at — 70°C.

B. D. Pullinger has continued her work on mammary cancer in RIII mice which develops without the operation of the milk factor. Ovariectomy in ageing mice did not increase the incidence or total number of benign or malignant growths, but "ovariectomy in breeders at 9 to 10 months old produced a 14-fold reduction in the numbers bearing benign growths." Of special interest is Pullinger's conclusion, derived from "the part played by œstrogenic stimulation in the evolution of spontaneous growths in the mouse breast," that "in the strain used the action of œstrogen was analogous to the action of a *promoting* factor on experimentally induced papillomata of the skin."

Experiments on surface X-radiation of the nipple area of the mouse have yielded 7 mammary carcinomas in 29 mice which lived longer than $11\frac{1}{2}$ months. The report says:

"It is highly improbable that any of these tumours were spontaneous, and none was associated with primary ovarian tumours. One striking change in the directly irradiated mammae was complete involution with atrophy and failure to respond to endogenous œstrogen. This appeared before there was any evidence that malignant tumour formation had started."

H. G. Crabtree has carried out experiments to test his suggestion that *p*-aminobenzoic acid may play a specific rôle in the induction of liver tumours in rats by certain azo dyestuffs. This suggestion sprang from his discovery that a series of non-carcinogenic azo compounds, all of which yielded *p*-aminobenzoic acid on metabolic breakdown, could significantly retard the rate of induction of liver tumours in rats by butter yellow or *o*-aminoazotoluene. An alternative interpretation assumes that the presence of additional azo compounds might retard the rate of metabolic rupture of the carcinogenic molecule by competing for the enzyme systems involved in this process. Crabtree has now prepared a similar series of azo compounds which, on metabolic breakdown, yield the corresponding sulphonic acid—sulphanilamide—instead of *p*-aminobenzoic acid. Four out of five members of this series of sulphur-containing azo compounds, when fed to rats together with butter yellow, delayed the time of appearance of liver tumours, compared with that in animals receiving butter yellow alone, by about 6 to 7 weeks. Sulphanilamide itself also had a similar retarding action on the development of tumours by butter yellow. The one sulphur-containing azo compound which failed to protect was found to be itself a weak carcinogen.

EUROPEAN LEAGUE FOR MENTAL HYGIENE

AT a conference of this body held in Rome from April 7 to 11 the main theme was the relation of mental health to public health—a subject that will also be discussed at the conference of the World Federation for Mental Health at Toronto in August.

In her presidential address, Dr. DORIS ODLUM (London) said that an important step towards mental health had been taken by establishing in many countries national associations for mental hygiene which could bring together representatives of every aspect of the life of the community. Yet in nearly every country a large proportion of the medical profession was among the opponents of the mental-health approach. Investigations (admittedly on a limited scale) suggested that, in England at any rate, some two-thirds of general practitioners either fail to recognise the neuroses and psychosomatic conditions or are so opposed to psychiatry that they never seek psychiatric help. There was great need for the better education of the public in the principles of mental health and in the great help that psychiatry can give to those who are mentally sick. A growing appreciation of the psychosomatic disorders was making it more obvious that mental and physical health cannot be separated; and "there is," said Dr. Odlum, "a tremendous demand on the part of the public for help and guidance in their personal problems."

Dr. J. R. REES (whose address was given in summary by his wife, Dr. Hemingway Rees) spoke of the need for partnership between mental health and public health. The World Federation for Mental Health (of which he is director) was composed of 50% professional associations and 50% mental-health societies coming from many countries. Part of its job was to encourage further research and better treatment; but we should never be able to provide treatment for all who need it, and the more important task was that of prophylaxis. The chief considerations included the upbringing of small children, the effects on small children of separation from their parents, and the effects of stress and anxiety leading to the development of psychosomatic illness. In all health education it was necessary to coöperate with colleagues whose primary concern had been with the prevention of physical disorders.

Dr. DONALD BUCKLE (regional officer for mental health of the European region of the World Health Organisation) said that the first task of education in this field was to bring the concepts of mental hygiene into the open. Without this change of outlook nothing could be effective. It was only because in some countries this educational change had already come about that we had seen the legislative changes which had created improvements in the treatment of the mentally sick.

Dr. ANDRÉ REPOND in his paper pointed out that it is very difficult for the principles of mental health to make headway against the deeply ingrained tendency of human beings to rely on magic, especially in relation to health. Those working in this field must not underestimate the unconscious emotional influences working against their efforts to develop human beings with well-integrated and harmoniously balanced personalities prepared to face and to accept reality.

Dr. P. SIVADON (France) said that after a long period of opposition and apathy in France there had recently been a considerable improvement in the official attitude towards mental-health concepts. Many of the ministries

now had psychiatric advisers who were called in for consultation and some even had psychiatrists permanently attached to them—e.g., the permanent commissions for health, for education, and even for housing. Prof. DE SANCTIS (Italy) described proposals by himself and Dr. Carlo Vetere, who was a public-health doctor, for furthering mental-health work in Italy. Dr. E. STENGEL (London) described investigations into the social significance of suicide and attempted suicide.

In the discussion, Prof. H. C. RÜMKE (Holland), president of the World Federation for Mental Health, said that we must beware of adopting the attitude of dictators in mental health and laying down the law. At present our knowledge of normal man was very limited, and had been obtained largely through the study of the abnormal. The time had now come when we could go out into the world and try to study, in company with our fellow men in every field, the workings of the mind and personalities of normal people. Thus we should hope to arrive at some real understanding of the factors concerned in producing mental health. Prof. HANS HOFF (Austria) replied that although it was true that there was much we did not know, we did in fact know a certain amount and could put it into action in certain fields. For example, we could advise mothers on the upbringing of their children, we could help young people with their emotional problems, and we could also give help and advice in relation to employment.

Medicine and the Law

Loss of an Eye

A CLAIM for £3000 damages against a former house-surgeon at Dundee Royal Infirmary was dismissed in the Court of Session by Lord Strachan,[1] although he found the doctor guilty of professional negligence.

The plaintiff was a girl who in March, 1951, at the age of 15 months, had fallen face downwards on a broken cup and injured her left eye. At hospital the house-surgeon found a laceration of the eyelid but failed to observe any injury of the eye itself and allowed the child to be taken home. When she was seen some weeks later by the family doctor the eye was found to be blind and it was afterwards removed lest sympathetic ophthalmia should affect its fellow.

The judge said that the expert evidence of seven eminent ophthalmologists had agreed that the defendant should have reported the case to a specialist. As to whether his neglect to do this had caused loss or injury to the child, his lordship held that, on the evidence, the doctor had established his defence that the condition of the eye was irreparable from the outset, and that no treatment could have made any difference.

Accidental Overdose of Insulin

At a recent inquest[2] at Sedgefield, co. Durham, the coroner recorded a verdict of accidental death on a woman who died after being given an injection of 5 ml. of insulin. The patient, who was under treatment for mental confusion, was being given 5 units of insulin daily. The sister in charge of the ward, who had been looking after the patient since her admission to hospital on Feb. 28, said she had instructed a nurse, who came on to the ward the previous day but who had had training in insulin treatment, to give the patient her usual 5 units of insulin on the morning of April 12. The nurse queried the dosage verbally and the sister, in evidence, said she thought "units" had been mentioned. The nurse stated in evidence that she had said "5 c.c.s.?" in an inquiring tone of voice, and the sister had replied "Yes." The patient was later found to be in coma and died despite attempts at resuscitation. The coroner said that he thought the sister stated the correct dose but that the nurse misheard her.

1. *Scotsman*, April 10, 1954; *Glasgow Herald*, April 10.
2. *Darlington Times*, April 17, 1954.

The Widdicombe File

XI. THE SAD TALE OF MRS. SMITH

The County Medical Officer of Health
DEAR DR. COBBLEIGH,

EVER since I settled in partnership here I have been meaning to ask if I might come to your office and introduce myself. Sir Daniel Whiddon showed me your letter about his farm and I was sorry I'd been so dilatory.

Since I qualified I've retained the impression that the public-health doctors are to be spoken to only in emergency or in protest, and district nurses and midwives are the only representatives of the service that I've actually met. But I'm beginning to realise that you and others provide my patients with services of which I'm still ignorant. And I'm wondering whether you can help me with my problem families.

I have about a dozen of them on my list, and they give me more trouble than all the rest put together.

This afternoon I've been visiting the Smiths, of no. 13 Downtown, who are in constant trouble with the diseases of dirt and ignorance. As a young and inexperienced doctor, with all my illusions still about me, I've tried to approach the family in the crusading spirit, as a challenge to preventive medicine and health education. But I've so far failed miserably and have for the moment retired, frustrated and fleabitten.

* * *

The central figure in the Smith drama is Mrs. Smith, known to her friends as Our Rita. She is 38 and has five children, a sixth on the way, and a seventh in the graveyard. She herself was one of a large family of kind and feckless parents, was fairly well fed but seldom washed, and grew up with little training or discipline other than the exasperated slap. She was educated at vast expense by the State, but her low intelligence and frequent absences from school prevented her from learning anything more advanced than to read the comics. After leaving school she drifted through various jobs in laundries and shops and eventually settled into quiet and unexacting employment sweeping out a large store. Here she learned from the other girls, who were kindly and rather brighter; following their ways she came under the magic spell of Hollywood and went to the Odeon twice a week, where she could enjoy luxurious surroundings and Romance in Glorious Technicolor for 1*s.* 3*d.* Following the example of the Stars, she took up Glamour in a big way, smartened herself up, used make-up, and was more or less clean. With some decent clothes, uplift, and a perm she fancied she might become a star herself if a talent scout happened to come her way, but somehow one never did. For the most part Hollywood was quite a good influence on Our Rita, although as she came to spend more time and money on her appearance than on food, she became poorly nourished and underweight.

At the age of 18, it seems, she met Bill Smith, a steady-going chap who worked for the council, digging holes in the road; as a result of some rather disappointing physiological experiments in a hayfield it became expedient for her to become Mrs. Smith, which was not so romantic as she had been led to expect. However, the baby which arrived six months after they were married left her little time to worry about that. After living with her in-laws for a while they were lucky enough to get a council house on a new estate. To begin with, Mrs. Smith was proud of her new house and tried to keep it nice, but as she had never learnt much about housekeeping and cooking she found this difficult. The baby was a great worry to her, and the unaccustomed responsibility and disturbed nights made her tired and irritable. She had ceased to care about her personal appearance soon after marrying Mr. Smith. When the second baby arrived, eighteen months after the first,

she had far too much to do and things got on top of her; the house became dirty and the cooking neglected. By a slow but unrelenting process of decay, accelerated by each childbirth, the Smith family became slum-dwellers.

It is easy for the stranger to pick out the Smith house. Most of the council houses in Downtown are well kept, with cheerful curtains in the windows and productive gardens. The garden of no. 13 contains a wilderness of weeds and a derelict perambulator; the gate is loose on its hinges, there are no curtains in the windows, and the washing on the line is dirty. On entering the door the visitor is assailed by a strong smell; there is a general appearance of dilapidation, and the floor and walls are dirty. What furniture there is, is falling apart, and the rooms are cluttered with dirty clothes and rubbish.

Mrs. Smith wears some ancient garments, which I can't describe and hope not to have to take off some day to examine her. She is anæmic, her teeth are bad, and she looks about 50, though she is only 38. She suffers from menorrhagia and abdominal pain, largely the result of coitus interruptus, and her varicose veins get worse with each pregnancy. She is by nature kindly, feckless, and uncomplaining. There are five children—Alf, Ern, Linda, Georgie, and Doreen—a sixth died of diarrhœa in infancy. They have runny noses and one or other of them is usually on my visiting-list for discharging ears, impetigo, or diarrhœa. They are dirty and their clothes are ragged, though adequate to keep out the cold. They are usually shod in rubber boots or canvas shoes; they become noticeably cleaner when they go to school and find themselves laughed at by the other children for being dirty.

They look surprisingly robust, though their diet is predominantly carbohydrate, with potatoes, cream buns, ice-creams, and chocolate high on the list; protein is supplied by school meals, the fish-and-chip shop, and a few eggs which the chickens in the back-yard sometimes produce. Mr. Smith provides £7 a week, is affectionate to the children, and believes in keeping out of the way as much as possible. About £4 a week and the children's allowance go to the house-keeping, the rest to beer, cigarettes, and the television set on the hire purchase.

* * *

That is the Smith family, resigned, dirty, but struggling along as best they can. They are good-humoured, generous, and in spite of everything likeable. The sordid state they live in is not due primarily to poverty, nor to housing difficulties, nor to lack of schooling, but to the unalterable fact that Mrs. Smith is of very limited intelligence and unteachable by ordinary methods. She is, in fact, a high-grade mental defective; and it's on her inability to learn that all efforts at preventive medicine come to grief. With considerable persistence she can be shown how to keep the house clean and the children cared for, but in a few weeks the family is back again in squalor, the new baby and the toddlers being fed milk out of an old beer-bottle with a rubber teat stuck on the top of it.

The health visitor, the district midwife, and the general practitioner share the task of trying to keep the Smiths out of trouble. I think the health visitor plays the biggest part; she has the special training in nursing and social work and can help Mrs. Smith over the shopping and the children's clothes. She understands the Smiths and is liked by them, so that she can keep up the pressure of benevolent nagging without offending them. I have met the health visitor in Widdicombe and discussed the problem families of the practice, to my great advantage. The district midwife is also on good terms with the family and helps them spring-clean the house before each new baby arrives. As the G.P. I have tried to show Mrs. Smith how to kill the flies with a D.D.T. spray and have given her ferrous sulphate tablets which she does not take. The most pressing need is to stop Mrs. Smith having any more babies, which would give her a chance to look after those she has already. I have fitted her with a dutch cap and spermicidal cream, but these she will not use and her husband considers his own methods of contraception good enough.

So far I feel that I have only scratched the surface of the problem, treating the various diseases of squalor as they appear. Probably the only measure which would alter the situation materially is to sterilise Mrs. Smith, to which I do not suppose either the Smiths or a gynæcologist would agree, and which I cannot persuade myself is really right; it carries with it a great danger of encouraging promiscuity and breaking up the home.

I am anxious to take Mrs. S. into the local G.P. maternity home for her next confinement, her seventh. She has reached a dangerous degree of multiparity and I don't want to find myself dealing with a postpartum hæmorrhage or prolapsed arm in no. 13 Downtown. If the children can be looked after for a while I would like to keep her in hospital for a good rest, proper food, and a course of iron and vitamins, and have her teeth seen to. At the same time we can enlist the help of Mr. Smith to clean up the house. Would your department be able to help with the children? A month's holiday at a children's home would do them the world of good.

But what can we do for the future? I suppose we should be thinking about the schooling of Mrs. Smith's daughters. They are no brighter than she is, and are not likely to derive any greater benefit from a formal State education. What they need is a simple training in the elements of house-keeping and mothercraft in a special school for the handicapped, if they are not to follow in their mother's footsteps.

I look forward very much to discussing all these problems with you, for I badly need a conducted tour of the Welfare State, which is confusing to the untutored traveller.

Yours sincerely,

W. BREWER.

Public Health

Infantile Gastro-enteritis in Exeter

DURING the eight months from July, 1953, to February, 1954, there were 21 cases of gastro-enteritis in babies under 1 year who were being treated in, or had recently been discharged from, the Royal Devon and Exeter Hospital. 6 of the babies were in the maternity nursery, and the remaining 15 were patients in the children's ward; but in only 4 of these 15 did the infection show itself in hospital. In the other 11, symptoms did not develop for periods ranging from a few hours to ten days after discharge; 7 of the 11 fell ill within two days. It may be that a few of these cases were infected after discharge. There were 3 deaths in the hospital, and 2 more babies died in an isolation hospital. In every fatal case there was some other substantial contributory factor which aggravated the infection: thus, 2 of the babies were grossly premature (3 lb. 4 oz. or less at birth). *Escherichia coli* 0·55 was recovered from 8 cases, and no other pathogen was discovered. Gastro-enteritis was prevalent in the area during the period and *Esch. coli* 0·55 was isolated from some of these outside cases. During the same period, apart from 4 children readmitted because of gastro-enteritis occurring after discharge, 4 cases of gastro-enteritis were admitted to the hospital, 3 of them in December (12 of the infections in infants occurred during December and January). These admissions may have kept the infection "alive."

The whole outbreak is an example of a creeping epidemic with a number of apparently disconnected episodes and, therefore, not readily recognisable at the time. Crowding of the maternity ward and nursery has caused anxiety for some time, and, on the advice of the pædiatrician and the hospital's standing committee on cross-infection, a small isolation unit for children and a small premature-baby unit are being provided by the conversion of certain rooms. The committee is also reviewing the whole outbreak, and a report is being prepared for the regional hospital board and the Ministry of Health.

In England Now

A Running Commentary by Peripatetic Correspondents

As a passive amateur of the arts I always envy the active amateurs who open the piano, ring up the curtain, or seize the paintbrush with their own hands. To this courageous body belong, of course, the members of the Medical Art Society, and judging by their exhibition (at Walker's Galleries, 118, New Bond Street, London, W.1, till May 8) they have all had an enjoyable year, with a good deal more to show for it than I have.

To begin at the beginning, Sir Philip Manson-Bahr, appropriately maintaining the equine tradition of another president, contributes a study of his black hunter *Merrymack*; and I also liked the feathered flurry of his *Ducks and Drakes*. The landscapes were varied and accomplished. I recall with pleasure Sir Harold Gillies's brown and white study of *Beech Trees in Snow*; the rust and grey roofs on T. M. Ling's *Beedingwood Farm, Sussex*; the flat placid pattern of church and water in R. Ogier Ward's *Friston Church*; the space and the snow of A. M. Rackow's *Cumbrian Farm*; the purple shadows of E. M. Whetnall's *Santa Barbara Mission*; the inviting turn of the street in Henry Wilson's *Standon Village*; the black figures of three Negroes walking down a near-black road in M. G. Corco's *Near Oji River*; the effectively scrawled red-ink roofs and roads of Isabel Wilson's wide countryside in *Flight over Europe*; and the path through a dark wood in Ian Robin's *The Glen*. Clearly there are some seafaring folk among the society; A. S. Till saw *The Blackwater at Malden* as a pleasing study in blues and yellow, and T. Holmes Sellors shows us furled rust sails at *Ipswich Docks*.

Among the portraits W. Hartston's studies of Africans stand out, especially the profile *Ahmed*. In Lady Whitby's *Freda* the red, white, and green of the figure is supported by a background of dull blue and pink. Denis Cronin has contributed several small sensitive bronze heads.

The still lifes ranged from N. Newman's pleasing but restrained vegetarian arrangement of two spring onions, two Spanish onions, two carrots, and three pea-pods, to the eerie assortment of fungi in J. F. Stokes's *Conference*. Norman Ashton suggests a satisfactory *Design for Living*: his simple bread and cheese and boiled egg stand beside a brilliant microscope, graceful glass flasks, and the ophthalmologist's bottle of atropine, and behind it all a beautiful decorated plate. Lady Whitby's bottle, mug, red book, and knitting-needles backed by grey rugs suggests a simpler but also attractive way of life.

The implicit social criticisms of these pictures is explicit in B. N. Brooke's *The Choice* (a woman faced with three hellish hats); and in M. Partridge's *Evening—North London* which shows Mrs. Battle of Golders Green at the bridge table. Nor has the new wirework trend been neglected, and in the *Unknown Political Stunt* S. Hales offers his views on the National Health Service. Cecil Ruben's *Bar at the B.M.A.* looks inviting, but I think the one at the Folies Bergère still has it.

* * *

My 2¾-year-old was drawing long lines all down her page. "This is a Zebwa Cwossing . . . but all the other animals can use it too."

* * *

I am still vaguely worried about Easter Monday. It was a beautiful sunny day and we all went to Plumpton Races. We got a good place for the car on the hill, just in time to watch the first race. Then I explained the horrors of betting to the boys, but said it was all right to put a small amount on a horse, if you could afford to lose that much, to give you an interest in the race. I had never backed a winner, I did not know the name of a single horse there, but I was going to put something on one for the second race, to have a horse to watch.

I had a newspaper which recommended Rowley Boy. Waiting my turn at the tote, I saw that one of the other horses was The Editor, and being an editor (of a small specialist journal) I put my money on him, and a very nice race he ran, winning the two-mile steeplechase by two lengths. After collecting 17*s.* 10*d.* I explained to the children that if one betted, which of course one shouldn't really, and was lucky enough to win, one must not let it go to one's head, and double up. I then departed to place a small-amount-that-I could-afford on Glim and Dim, the paper's selection for the next race. With ten seconds to spare I discovered the horse was not running, and glancing like lightning down the card, I saw that Athelney, very near my mother's old home in Somerset, had that lucky number 13. This fortunate coincidence brought me 16*s.* 2*d.*, although I had been watching the wrong horse as Athelney's jockey's colours looked sea-green instead of turquoise. I explained to the children that it was wrong to be carried away by betting, that two was a coincidence, but it took three to make a syndrome, which I hoped they would think was a particularly wicked sort of sin.

I had to leave rather hurriedly to place my bet on the next race, the Abergavenny Challenge Cup, but I saw that there were only six runners and reasoned that each of them had a chance of a place. I selected Nome, as for years I wanted to go to Alaska. He turned out to be a lovely dark slim creature, frisky and heartening. He had the inside place, got the lead, and kept it. The favourite challenged him in the last half-mile but fell. Refreshed by this little coup (£2 0*s.* 8*d.*), I determined to lose next time by backing the outsider, Distani, but found my wife had the same idea and so gave the newspaper expert another chance—Diego Rubio was his choice. Distani, a little horse, led to start with, but of course Diego Rubio won.

I started to tell the children about betting, &c., but caught a cynical look in the eye of the eldest, and shut up. He said that he was going to bet this time, on Never Again (by Boozer's Gloom out of Officers' Mess). I declared for either Western Slipper or Windsor Light, but as I approached the tote window I thought everyone who wasn't on either of them was on Le Serpent, so I simply backed the favourite, Retlaw, and went to watch the race. The issue was at no time in doubt. Never Again was second.

The real tragedy is that I didn't double up, but what worries me is that although I don't know enough to work out whether picking five winners in a row is statistically significant, it looks it. And if it is, there is something queer about statistics, considering my methods of choosing winners. Perhaps the real solution is that there is something queer about racing. The only conclusion I can draw is that if you follow your nose you and your family may have a day at the races for nothing. Of course you must have the right nose, like those chaps with clinical intuition.

* * *

Whether Her Majesty's Government would consider helpful advice from the U.S.A. to convert the alleged loss of the second battle of Trafalgar [1] into a victory, or at least a stalemate, I don't know. But I venture to draw their attention to a recent communication on the Use of a Specific Sound to Repel Starlings (*Sturnus vulgaris*) from Objectionable Roosts.[2]

The authors found that when starlings were held by the legs or wings, they emitted a piercing shriek. This distress call caused other starlings to leave their roosts and not return even after some months. This suggested that a recorded distress call might be used as a repellant. Accordingly, wild starlings were induced to give distress calls by holding their legs and shaking them roughly. The calls were recorded with a tape recorder. When the distress call was broadcast a heavily infested roosting area was cleared in 4 nights.

But I'm not clear whether that segment of Her Majesty's Government that has to maintain the traditions of Trafalgar, Nelson, et al. would consider a victorious end worth the employment of such one-sided means as holding the starlings' legs and shaking them roughly; or would agree with my implied classification of Trafalgar Square and appurtenances as "objectionable roosts."

* * *

Diagnosis in the Bus Queue

1ST LADY: "Have you been to the doctor's yet?"

2ND LADY: "No, not exactly. You see, I'm goin' an' I'm not goin'—that's how I am."

1. *Lancet*, Feb. 27, 1954, p. 463.
2. Frings, H., Jumber, J. *Science*, March 5, 1954, p. 318.

Letters to the Editor

THE BOMBS

SIR,—Many of your readers had been eager to hear your comments on the situation revealed by the recent "successful" experiments with hydrogen bombs; but some of us were conscious of an element of disappointment in our reactions on first reading your leading article of April 17. You did not try to present us with an analysis to which we could expect a large majority of our profession to agree. You did not put before those who crave decision and action a clear-cut choice between a heroic disarmament and an all-out support of the American policy of "negotiation from strength." You did not even encourage us to believe that members of our profession have as such no special duty in this matter.

But you did remind us that doctors are accustomed, more than most people, to face the facts of a dangerous situation realistically, and to do their best for everyone involved in the danger; and that a realist need not be a cynic. Realists who point out that war, having lost its survival value, is unlikely itself long to survive, seem to be on unassailable ground; the trouble is that it may nevertheless survive long enough to destroy all that we value in our world, and perhaps life itself.

Dr. Duncan Leys and Dr. Alex Comfort, in their letters last week, express grave doubts about the emotional balance of those in control of thermonuclear research in America. Dr. Leys thinks that "neither fear of retaliation nor any moral considerations will restrain the desperate"; he implies that those in effective control of thermonuclear weapons in the U.S.A. are, or may become, so desperate with guilt-ridden fear as to be inaccessible to any rational restraint; and there is evidence to support such a view. At least there can be little doubt that ever since the comparatively harmless pioneer atomic bombs were dropped on Japan there have been evidences of abnormal guilt-reaction in America. The danger of the devastation of Britain by hydrogen bombs or other thermonuclear weapons is vastly greater than the corresponding danger in America, while the fear-reaction is greater in America.

Dr. Comfort uses the ugly word "paranoia" in referring to the mentality of those who inspire and direct these activities; similarity between the emergent action and that recognised in individuals as paranoid is certainly striking. There is the same persisting terror of persecutory aggression, the same unrestrained violence of defensive response to it, the same effective planning in complete secrecy. It will be said that the paranoid protects himself against non-existent dangers, while the enmity directed against the U.S.A. is real; and there is evidence of emotional imbalance in Russia too. However true this may be, it emphasises beyond everything else the need for the sane and benevolent forces in the world to assert themselves.

It is common knowledge that when all are afraid, as before the outbreak of a panic, those who are most afraid take the lead. I have become accustomed to think of fear and flight as the least worthy emotional reaction to danger, with escape to anger and counter-aggression as a more admirable, as well as a more comfortable, alternative. It is perhaps unreasonable to expect a group which has risen from fear to successful aggression voluntarily to abandon a security based upon fighting strength in favour of a greater security which may have the appearance of weakness. But the urge to survival, applied through the less frightened and more rational members of the community, may supply the necessary compulsion; and there is for the individual, and no doubt for a nation, a stronger defence than counter-aggression. If he can find courage enough to study, without preconceived fear and enmity, the motivation of his enemy, he can usually—not always—find so much in common with his own that the mutual enmity is mutually disarmed, to the benefit of everyone concerned.

Those who have never used this method cannot be expected to value it, but they might nevertheless be ready to see that pride in fighting-strength may not be the final consideration in human values. It seems that the time has come to revise that valuation, in the interests of our friends and of our enemies as well as in our own. Personal pride, classified by Aristotle as a virtue, is a vice by Christian standards; national pride may be due for a similar revaluation. I like to feel still at liberty to be proud of our national achievements, and I would certainly find conquest from abroad more offensive if the occupying troops were non-English-speaking; but I should like to place it on record that if given the choice between this and victory over the foreigner by the snuffing out of his civilian population I should hope and expect myself to choose the former.

London, W.1. J. NORMAN GLAISTER.

SIR,—Dr. Comfort's letter based its main argument, however sincerely, upon a major misconception. No matter how much one may detest war and desire reconciliation between nations, it is sheer speciousness to infer that for Britain there is less menace from Russia than from the United States. The North Atlantic Treaty Organisation is probably the only thing that has stood between Russia and the subjugation of Western Europe, and to attempt to confuse this particular issue is to play into the hands of Communist propaganda. Quite apart from this, it is a matter of historical fact that it was the United States who proposed, and still propose, international control of the production and development of atomic weapons, while the Soviet Union have consistently refused to accept such control.

For Britain now publicly to dissociate herself from her greatest ally—for that is what Dr. Comfort's proposition would in fact amount to—would be to present the world as a free gift to tyranny. *Of course* we must continue to press for international control and inspection of all atomic weapons, with a view to their ultimate abolition—and we should be well advised to extend this to submarines and rockets, both of which are the subject of intensive Soviet research and would be obvious weapons to deploy against our island. More important still, we must do all we can to achieve a permanent reconciliation between nations. But to suggest in this context that we have no more reason to trust the United States than the Soviet Union is precisely the kind of misguided propaganda which Dr. Comfort so rightly deplores.

Guy's Hospital, London, S.E.1. DAVID STAFFORD-CLARK.

SIR,—I wonder how many people really believe that the hydrogen bomb is a blessing in disguise, that it presents a compelling safeguard beneath a horrible threat? Politicians in plenty are expressing this curious idea, and Professor Haddow's appeal to a more enlightened section of society is amply justified on this ground alone. The potential blessing of so uncontrollable a weapon will surely escape the comprehension of men and women who have been nurtured on Christian ethics and Greek culture. The humanitarian professions, then, are armoured against such dangerous heresies; it is mainly from them that any resistance to a universal moral landslide must derive.

There must be many within medicine and its outlands who, having long held that the desperate state of human affairs has sprung from a lack of religious faith (Christianity in particular), now see a second cause—mental aberration. Dr. Comfort is one of a great company who hold this a very serious development. The priest and the psychiatrist must now work hand in hand for the healing of the nations. All who face the ideal of physical, mental, and spiritual health must find a new poignancy

in the situation, for today the power of a psychopath in a high place is such that he need ask no man's leave before he precipitates horrors.

There are millions of sane and charitable human beings whose endurance must outlast that of Damocles. Most of them are lonely and inarticulate; they derive new hope and vigour from any who will stand up and voice their fears for them, and convince them that their thoughts are in fact being broadcast and therefore not hopelessly drowned in the shouts of maniacs. There is some sort of moral obligation upon those professional men and women who believe that mankind must settle its disputes peacefully to express the goodwill and the moral scruples of the inarticulate, for theirs is the authority and the ability, by reason of the service they render to society. Only if such men and women accept this responsibility and act upon it, will there be mobilised a force capable of outlawing war itself and seizing, at this eleventh hour, our one chance of civilised survival.

Pharmaceutical Department, Southmead Hospital, Bristol. PETER COOPER.

TUBERCULOSIS YARDSTICKS

SIR,—Dr. Stewart and Dr. van Zwanenberg, in their letter of April 17, have drawn attention to a difficult and topical problem—namely, the criteria which should now be adopted in assessing the "activity" of a case of pulmonary tuberculosis. They suggest that assessment must depend largely on the results of bacteriological examination, but they then proceed to produce some evidence which implies that bacteriology is no longer wholly reliable. We are certainly becoming increasingly familiar with the patient who presents the X-ray appearance of cavitation coupled with an impressive series of negative sputa, and as a result the *cachet* formerly conferred by the production of a negative culture or animal inoculation test has lost a little of its lustre. It is perhaps going too far to say that such desirable bacteriological findings can be produced at will by juggling about with the chemotherapy; but they can be influenced very appreciably, and consequently negative bacteriological findings should now be accepted with great reserve, unless the clinical and radiological evidence is completely in keeping.

In the official definition of quiescence pride of place is given to improvement in the patient's general condition, to the absence of toxæmia, and to negative sputum examinations, while the evidence provided by other clinical examinations and by serial radiographs brings up the rear. A readjustment of these criteria is overdue; and, while all the factors mentioned should continue to be given adequate consideration, increasing emphasis might with advantage be placed upon the radiological findings, including tomography, which at present appear to be the most reliable index of potential infectivity which we possess.

If the number of patients admitted to hospital for the treatment of pulmonary tuberculosis, who have received chemotherapy before any attempt has been made to confirm the diagnosis by sputum examination, can be accepted as a guide, then the popularity of bacteriological investigation has declined even further than many of us would have supposed.

Red Cross Sanatoria of Scotland, Tor-na-Dee, Milltimber, Aberdeenshire. R. Y. KEERS.

TUBERCULOSIS IN ADOLESCENCE

SIR,—Most of the measures Dr. Bentley suggests in his letter last week are, of course, long overdue, largely because the dangers of an unrecognised primary infection during puberty are not always appreciated, because the value of B.C.G. in preventing adolescent phthisis [1 2] is underrated, and because the relative rarity of the disease is allowed to conceal its importance. (In England and Wales 3–9% of children dying between the ages of 10 and 14 years do so as the result of respiratory tuberculosis.) Incidentally, the "inevitable deterioration" mentioned by Dr. Bentley is distressingly obvious in recorded experience of the disease: half the patients used to die within 2 years, and three-quarters within 5 years, of diagnosis.

The use of tuberculin testing before mass radiography is obviously rational, and probably economical. It should prevent the false sense of security sometimes engendered by a report that the chest radiograph is normal in a tuberculin-negative adolescent. The measures suggested (tuberculin testing, radiography, and vaccination) may be criticised as impracticable, uneconomical, and unnecessary. But they would certainly be more rewarding than, for example, the prolonged surveillance of healthy tuberculin-positive children between the ages of 5 and 10 years, still practised in many centres. Moreover, disease discovered at the asymptomatic stage is likely to be amenable to treatment within a reasonably short time, thus avoiding the expense of a long stay in hospital (providing too sanguine a view is not taken of minimal lesions [3]). Furthermore, the final years of school life are the last occasions when all the youth of the country is readily available for epidemiological study and the practice of preventive medicine on a large scale.

Dr. Bentley's suggestions should be implemented first in girls' schools, for phthisis is 3 times more common in girls than in boys between the ages of 13 and 15 years.[4]

In North-eastern England most children who develop this adult type of pulmonary tuberculosis are treated at one centre (Poole Hospital, near Middlesbrough). Here, as recommended by the National Association for the Prevention of Tuberculosis,[5] the children's hospital is not isolated, but is an annexe of the main establishment, which is fully equipped for thoracic surgery. A recent survey [6] of cases seen at this centre showed that early diagnosis and themotherapy, combined with rational collapse and surgical procedures, have more than trebled the immediate expectation of life in childhood phthisis. But prevention is still far better than cure.

Bishop Auckland. J. P. ANDERSON.

CANADIAN APPOINTMENTS

SIR,—Your issue of March 27 contains an advertisement for a consultant post in Canada at a salary of $10,000 per annum. The notice indicates that this is approximately equivalent to £3700 sterling.

I feel strongly that prospective candidates for the post should be made aware that in terms of living standards $10,000 is equivalent to nothing like that sum. The present rate of exchange ($2.80 to the pound) is unrealistic; to provide a closer approximation to reality a figure in the region of $5.00 should be cited. This post, which appears to be far more highly remunerated than one of equal status in England, is thus very much on the same level. $10,000 will provide a reasonable standard of living, but it is far from wealth: radiologists in private practice in this country can make two to three times that figure and commonly do so.

This is not the first advertisement in *The Lancet* to mislead British doctors with ambitions to emigrate by proffering apparently generous salaries in terms of dollars; but I believe it is the first to translate dollars into pounds in this way.

1. Hyge, T. V. *Acta tuberc. scand.* 1949, **23**, 153.
2. Wallgren, A. Tuberculosis and other Problems of Pediatrics. Baltimore. 1950.
3. Anderson, J. P. *Lancet*, 1952, ii, 490.
4. Anderson, J. P. *Ibid*, 1952, i, 876.
5. National Association for the Prevention of Tuberculosis. Design for Sanatoria. London, 1951.
6. Anderson, J. P. Phthisis in Childhood. M.D. thesis, University of Durham, 1953.

I would therefore urge, Sir, that some editing of Canadian advertisements be made, or that the large difference in the cost of living be drawn to the attention of applicants. M.D.

Canada.

*** A similar letter of warning about the cost of living in Canada appeared in our issue of Sept. 27, 1952 (p. 640). —Ed. L.

RHEUMATOID ARTHRITIS AND ALLERGY

SIR,—The inter-relationship of rheumatoid arthritis and various allergies has often been discussed, and any such claims have usually been rejected, as was the case of the statistical investigation by the Empire Rheumatism Council in 1950. The alternation, however, of various allergies, the duodenal syndrome, and psychoneurotic states is, I believe, not uncommon.

In an examination of the case-histories of 1000 rheumatoid arthritics, 6 were found in whom the arthritis began at exactly the time that an asthmatic state disappeared. Unfortunately, not every patient was specifically questioned about the presence or absence of any asthmatic tendency, and therefore no data are available about the incidence of asthma in this series. The occurrence of 6 cases in which rheumatoid arthritis appeared to replace the asthmatic state is of interest and seems to merit further investigation by others when analysing future series of cases. We would be very grateful to hear from anyone interested in either the rheumatic diseases or psychosomatic and allergic conditions, whether their experience confirms or refutes this finding.

Rheumatism Research Unit of the South West and Oxford Regions, Royal National Hospital for Rheumatic Diseases, Bath. G. D. KERSLEY.

AVERTING POLIOMYELITIS

SIR,—Now that the threat of poliomyelitis is again upon us, may I, like Cromwell, beseech you, in the bowels of compassion, to think it possible that it may be averted?

These facts are authoritatively stated:

(1) "Poliomyelitis is an infection of the lining of the bowel, prone to pass more deeply into the body." [1]

(2) "Infection is only occasionally manifested by nervous illness." [2]

(3) "There is now agreement that poliomyelitis is essentially spread by human contact and that stools form the main source of the virus." [2]

(4) "Human fæces are the most significant source of the virus; the period of communicability may extend for longer than a few days after onset; the mouth is the usual portal of entry." [2]

The secret of the control of poliomyelitis is to make sure that all who are at risk from contact with a known case, direct or remote, shall have clean fingers after emptying their bowels. Anyone with a lump of wet mud and a piece of toilet paper can demonstrate how toilet paper is permeable to moist fæces and must allow the fingers to be contaminated at defæcation. One way to keep the fingers clean is to substitute cotton-wool for toilet paper or to use toilet paper in three thicknesses. Another is to use an effective antiseptic. The virus of poliomyelitis "is readily destroyed by oxidising agents such as hydrogen peroxide and potassium permanganate," [3] and an ounce of permanganate crystals, costing 5*d*. will make fifty gallons of potent solution. I suggest that by the side of every school and public lavatory in a threatened area we should place permanganate solution in 3-lb. jam-jars. On the toilet paper should be printed some simple words such as these:

This district is threatened with the disease called poliomyelitis. The germ that causes this illness lives in the bowels of ordinary men, women, and children, but only a few of them become ill. These germs are so small that they can easily get through a piece of toilet paper, so use it in three thicknesses. Then dip your hands in the jar of red water by the lavatory seat for a few moments. Then with wet hands pull the chain and open the door, and go and wash them thoroughly.

The matter could be made an interesting subject for science lectures in schools. Science masters and mistresses and their pupils should undertake the meticulous management of school lavatories; there is nothing degrading in fighting the causes of death and crippledom, and there need be as little sentiment on this subject as there is on any other part of the sewage system. Above all there should be the enthusiasm of a campaign—a campaign for a season, against a known enemy and with clearly defined methods of confining it.

In the broad stream of infection by poliomyelitis few are stricken: if we narrow the stream, fewer will be stricken; in the presence of a virulent strain this narrowing is a matter of grave urgency.

Beckley, Rye. C. G. LEAROYD.

TREATMENT OF VARICOSE ULCERS

SIR,—I agree with Dr. Rivlin (April 17) that the key to success in healing gravitational ulcers is adequate elastic support, but the elastic support need not be maintained by an adhesive bandage. Over ten years ago, woven elastic web bandages were introduced in our department by my colleague, Dr. H. R. Vickers, and we have found that they have all the advantages of an elastic adhesive bandage with none of the disadvantages of skin sensitisation or the sweat-retention syndrome.

The bandages are put on like a puttee from toes to calf; they have the advantage over elastic stockings that at the part where most support is needed, around the malleoli, extra turns of bandage can be applied if necessary, and any form of dressing can be used on the ulcer area.

One important feature is that most patients will continue to wear the bandages after the ulcer has healed. They come to look on them as a talisman which keeps the ulcers away, and the relapse-rate is considerably cut down.

I have never been able to discover why these bandages have not been used more generally in this country.

Rupert Hallam Department of Dermatology, Sheffield. I. B. SNEDDON.

SIR,—May I reply to the letter from Mr. Murley (April 10)? In doing so, I shall be replying too to Mr. Roland Jones and Dr. Rivlin (April 17) and Mr. Rowden Foote (April 24).

Firstly, there is the question of arterial spasm accompanying a deep thrombosis. I believe that arterial spasm does occur in deep thrombosis, and my belief is based on clinical observation.

I have observed that, in many patients giving a history of deep thrombosis from whatever cause, the toes are often cold and blue, indicating diminished blood-flow to the periphery. I have also found that there is very often a poor femoral pulse, and in some cases no pulse at all. Furthermore, I have sometimes been unable to introduce a fine needle into the artery, when attempting to inject tolazoline ('Priscol'), because the vessel was too small. Again, to prove that arterial spasm does exist, I have performed a clinical test in many cases. A skin thermometer is applied to the thigh and another to the dorsum of the foot; and the intra-arterial injection of tolazoline is then given. In nearly all cases the thermometer on the thigh shows a rise in temperature, and a great many show a rise in temperature in the foot as well.

The second point Mr. Murley raises is the question of lumbar sympathectomy for varicose ulcers. I myself have never done this operation for varicose ulcers, and in my letter of April 3 I do mention that, in the often

1. Burnet, F. M. *Brit. med. Bull*, 1953, **9**, no. 3.
2. Rhodes, A. J. *Ibid.*
3. MacCallum, F. O. *In* Viruses and Rickettsial Diseases. London, 1950.

fat and flabby patient who has a varicose ulcer, a lumbar sympathectomy would not be without its risk. But lumbar sympathectomy does (and Mr. Murley will, I am sure, agree with me) raise the temperature of the limb. The first answer I get from a patient who has had a successful lumbar sympathectomy always confirms that the limb feels warmer. It is also taught that sympathectomy has its maximum effect in dilating the skin vessels as opposed to the vessels of the muscles and other deeper structures. Surely an increase of skin blood-flow will promote healing of skin ulcers? Tolazoline will temporarily have the same effect as a lumbar sympathectomy.

Mr. Murley's third point is the question of pain in leg ulcers. I have observed that in many women the pain is worse before ulceration has occurred. The pre-ulcerated leg feels hard and brawny in its lower third, and sometimes the pain is so severe that the patient is reluctant to let anyone touch the leg. In contrast to these painful brawny legs ("inverted Guinness-bottle legs") there are those with considerable ulceration where pain is slight or even absent. Surely it is the strangulation of the leg inside the resistant skin which is giving rise to this dreadful pain.

Finally, I would like to say something about skin-grafting of ulcers. One has to be guarded in saying how long a graft will last, for many do break down sooner or later. The darn graft which I have mentioned elsewhere, and which I believe originates from an idea of Mr. Dickson Wright, has a place in the treatment of varicose ulcers. Its main use is in those ulcers which are wide in area and which are not punched out. The punched-out ulcer, on the other hand, is more difficult to heal, and should respond better to hyaluronidase plus injections into the femoral artery. I must make it clear that I advocate this treatment only when compression bandaging is not having the desired effect. As I said in my letter, firm bandaging still remains the basis of all treatments, and it is when healing is slow or non-existent that I advocate these extra measures.

London, W.1. MAURICE LEE.

SPONDYLOSIS

SIR,—In his Heberden oration, published in your issue of April 3, Sir Russell Brain has given a brilliant exposition of disc lesions at the different spinal levels. He draws particular attention to the dural root-pouch—an important structure in explaining symptoms. Clinical grounds had enabled the presence of this pouch to be inferred [1] and the deduction drawn [2] that at lower lumbar levels the investment is not less than an inch long.

Sir Russell points out that disc lesions give rise to pain that appears to follow the myotome rather than the dermatome, but this is not the full explanation. Dural reference is often entirely extrasegmental and, when pressure is exerted on the dura mater, the symptoms often spread far beyond any relevant myotome. Thus, an early cervical disc lesion at any level may give rise to pain spreading to the head (C1–2 dermatomes) no less than to the scapular area (T3–6 dermatomes). Similarly, the pain arising from the dura mater [3] in lumbago caused by, say, a 5th lumbar disc lesion, often reaches to the mid-thorax posteriorly, or to the abdomen, or to the groins, or to the coccyx, or to any aspect of the lower limbs. This represents reference far beyond both dermatome and myotome.

When the protrusion moves a little to one side, the dural investment of the nerve-root comes to be compressed. Now segmental reference appears, occupying the myotome proximally and the dermatome distally. By contrast, impingement on a nerve-trunk seldom gives rise to any local symptoms at all. Constant pressure leads to a painless paresis; intermittent pressure to distal paræsthesiæ (most severe during a period of recovery), in due course followed sometimes by vague aching in the affected limb.

This difference in the order in which symptoms appear provides a useful pointer in diagnosis; for pressure on dura mater and then nerve-root leads to pain in the trunk (though often in the "wrong" place), later spreading to the limb, whereas local discomfort is absent when a nerve-trunk is compressed.

The practical lesson to be drawn from Sir Russell's research on cervical myelopathy is that cervical and thoracic disc lesions are potentially dangerous. Hitherto it has been the practice to leave early protrusions to themselves, to get larger or smaller as fortune dictates. If, however (as has been the practice at St. Thomas's Hospital in our department for the last ten years), all cervical and thoracic disc lesions are reduced early on—when reduction is easy—the posterior longitudinal ligament escapes prolonged stretching and the likelihood of eventual myelopathy will clearly be diminished. Careful manipulation without anæsthesia during traction scarcely ever fails when the protrusion is small and recent, and it now appears to be not merely the useful pain-relieving measure I have so far regarded it as, but of far greater importance in the prophylaxis of eventual crippledom. Happily, therefore, Sir Russell's research points to an immediate therapeutic application.

London, W.1. JAMES CYRIAX.

1. Cyriax, J. *St. Thom. Hosp. Rep.* 1949, 5, 68.
2. Cyriax, J. *Orthop. Med.* 1954, 1, 382.
3. Cyriax, J. *Lancet*, 1945, ii, 426.

CLINICAL TESTS FOR KETONURIA

SIR,—The article by Dr. Nash and his colleagues in your issue of April 17 cannot be allowed to pass without comment. They describe the advantages of a tablet test for ketone bodies in the urine, and this is a praiseworthy contribution to chemical pathology. But they think it necessary to introduce a contrast by decrying the ways of discovering ketonuria used hitherto.

They state that there is uncertainty as to whether the colour given by the nitroprusside reaction is due to acetone or due to aceto-acetic acid. It has, in fact, been known for many years that the colour in the test is given by both compounds, but that the sensitivity of the test was such that it gave stronger reactions with aceto-acetic acid. Hurtley gave an elaborate account of the tests for acetone and aceto-acetic acid in *The Lancet* in 1913.[1] He pointed out that the Rothera test was about 20 times more delicate for aceto-acetic acid than acetone. Cole,[2] in the 5th edition of his book on *Practical Physiological Chemistry*, states that acetone can be detected at 1 : 20,000 and aceto-acetic acid at 1 : 400,000.

The authors find that the Rothera test is too sensitive. Kennaway showed in 1913 [3] that the speed of colour development depended on the aceto-acetic acid concentration. If this was 1 part in 200,000, the pink colour did not appear for some minutes. Ever since, it has been accepted that what Kennaway called the "slow-weak" reaction (i.e., when the colour does not appear for some minutes) was of no clinical importance.

The statement that Harrison [4] does not "indicate that the urine must be saturated with ammonium sulphate to give the maximal sensitivity" is incorrect. He explicitly writes: "Saturation with ammonium sulphate removes interfering substances making the test more delicate."

Dr. Nash and his colleagues say that few textbooks adequately describe the details of Gerhardt's test: in fact, Harrison's textbook,[4] which is only one among many, states the exact strength of ferric chloride to be added in the test—namely, 10%—and the quantity is described as "sufficient

1. Hurtley, W. H. *Lancet*, 1913, i, 1160.
2. Cole, S. W. Practical Physiological Chemistry. Cambridge, 1919.
3. Kennaway, E. L. *Guy's Hosp. Rep.* 1913, 67, 161.
4. Harrison, G. A. Chemical Methods in Clinical Medicine. London, 1947.

drops to be added to completely precipitate the phosphates." It is well known that any excess of ferric chloride is liable to render the test insensitive. In the same textbook it is said that boiling is to be *thorough* (italics by Harrison), and it is specifically stated that it should be done in a boiling-tube or open vessel. If the writers are correct (and we are prepared to doubt this) that the boiling is usually done only momentarily in a narrow test-tube, this would be quite contrary to the established descriptions of the technique. A recent article [5] goes as far as emphasising the need for prolonged boiling by prescribing a 50% evaporation.

We are looking forward with interest to the advantages of the tablets described, but we maintain that the present tests for ketonuria are effective, and also that, as far as we know, they are adequately performed throughout the country. The tablet test appears to be in fact a "dehydrated," slightly less sensitive Rothera test. If this was so, it would have no advantages in the laboratory but might be found to be convenient in the consulting-room.

Department of Pathology,
St. Bartholomew's Hospital,
London, E.C.1.

H. E. ARCHER
H. LEHMANN.

SIR,—In an otherwise excellent and informative article Dr. Nash and his colleagues seem to have overlooked a simple expedient for reducing the sensitivity of Rothera's test—namely, dilution. A 1 in 5 dilution of urine brings the test into the desired range of sensitivity and, for students, perhaps this is a useful manœuvre. In practice, however, the rate of colour development is a sufficiently reliable index for the experienced.

Secondly, no mention is made of the use of a crystal of sodium nitroprusside, which, as far as I know, is reliable, is certainly simpler, and probably saves several seconds.

Department of Clinical Pathology,
St. Thomas's Hospital,
London, S.E.1.

H. E. M. KAY.

PRESCRIBING AUREOMYCIN

SIR,—I wonder how many of your readers in hospital practice know that aureomycin cannot be prescribed by the general practitioner except by a very devious route—a restriction which applies neither to erythromycin nor to chloramphenicol. The effect can only be to further the use of an antibiotic known to be associated in some cases with the development of blood dyscrasias,[6] where antibiotics carrying no such risk are equally effective. The continued existence of this regulation is a matter of grave concern.

Wallington, Surrey.

H. BARRIE.

NURSING BY THE MOTHER

SIR,—Dr. Lowenfeld, in her letter of April 10, urges the need for fresh and creative thinking on the treatment of sick children in hospital. The Nuffield Provincial Hospitals Trust shares this view and has, in fact, initiated a study on the care of children in hospital. This study will be made on behalf of the Trust by the Nuffield Foundation's Division for Architectural Studies, the establishment of which was announced in your issue of Feb. 6 (p. 319).

This study of the child in hospital will follow the lines established by the Trust's investigation into the functions and design of general hospitals. These were similar to those suggested by Dr. Lowenfeld—that is, preliminary research by a team of people with appropriate experience, followed by experimental building to test and demonstrate the conclusions. It is hoped that work on this project will begin in the autumn of the present year.

London, N.W.1.

L. FARRER-BROWN
Director of the Nuffield Foundation.

5. Archer, H. E. *Brit. med. J.* 1953, ii, 1211.
6. Hodgkinson, R. *Lancet*, Feb. 6, 1954, p. 285.

Obituary

WILLIAM HENRY SNYDER NICKERSON

V.C., C.B., C.M.G., M.B. Manc., D.P.H.

Major-General W. H. S. Nickerson, a former director of Army Medical Services in India and one of the distinguished band of medical holders of the Victoria Cross, died at his home at Kintyre, Argyllshire, on April 10.

He was born at New Brunswick, Canada, in 1875, the son of the Rev. D. Nickerson. He came to this country to go to school at Portsmouth Grammar School, and to study medicine at the Victoria University of Manchester, where he graduated M.B. in 1896. Two years later he joined the R.A.M.C., and he served in South Africa from 1899 to 1902. He was repeatedly brought to notice for good work done under fire in the battle of Stormberg and elsewhere, and in 1900 he was awarded the V.C. and promoted captain. The following citation describing the award appeared in the *London Gazette*:

"At Wakkerstrom on the evening of 20 April 1900 during the advance of the infantry to support the mounted troops, Lieut. Nickerson went in a most gallant manner, under a heavy shell and rifle fire, to attend a wounded man, dressed his wounds, and remained with him until he had him conveyed to a place of safety."

In 1909 he received his majority, and during the 1914–18 war he served at first in France, taking part in the retreat from Antwerp and in the battles of Ypres, Neuve Chapelle, and the Somme. In 1915 he was transferred to Salonika and later he served with the Egyptian Expeditionary Force as D.D.M.S. For his war services he was appointed C.M.G. in 1916, and C.B. in 1919. He also received the Greek Medal for Military Merit.

His promotion had been rapid, and he attained the rank of major-general in 1925 at so early an age that he was allowed to postpone his retirement for four years, during which he served as director of medical services in India. When he retired in 1933 he was made colonel commandant of the R.A.M.C., an office which he held till 1945. During the late war he was medical officer to an Atlantic convoy, to the Port of London Authority River Emergency Service, and with the Home Guard.

A colleague writes: "It was most fortunate that Nickerson was appointed director of medical services of the Army in India when he was, because it was largely due to his influence that exceptionally cordial relations were established between the civil and military medical services. But for this it would not have been possible to offer so effective a resistance to the attack made on both services by the retrenchment committee set up to cope with the severe financial crisis which occured during these years. Insidious attempts were made to encourage and exploit conflicts of interests between the two medical administrations, both of which owe a great debt of gratitude to Nickerson for the part he played in their united defence of the policy of maintaining an adequate reserve of medical officers in India. Like the other medical friends of mine who have won the V.C., he was modest and unassuming, and utterly incapable of harbouring unworthy feelings of personal vanity. His selection on his retirement for the coveted distinction of colonel commandant of the R.A.M.C. reflected the affectionate esteem in which he was held by his fellow officers, and indeed by everyone who knew him well."

Major-General Nickerson married in 1919 Miss Nan Waller, who survives him with a son and daughter.

HAROLD PARNELL JAMESON

M.D., B.Sc. Birm., M.R.C.P.

Dr. H. P. Jameson, consulting physician in geriatrics to St. Albans City Hospital, died on March 31 at the age of 50.

In 1925 he graduated M.B. with first-class honours at Birmingham University, and after holding house-appointments at the General Hospital and Children's Hospital in Birmingham he moved to London, where he worked under Sir Robert Hutchison at the London Hospital and at Great Ormond Street. In 1928 he proceeded to the degree of M.D., choosing as the subject of his thesis the Remote Prognosis of Pneumonia in Childhood.

In 1929 he settled in practice at St. Albans with Dr. J. W. Hope Simpson, largely because of the opportunity for pædiatric work offered by the children's beds at St. Albans City (then Osterhills) Hospital. He had full clinical charge of these beds for ten years, and the new children's block was built under his direction.

For many years he was medical officer to the Honourable Artillery Company, and a week before the outbreak of the 1939–45 war he was called up. He served in India, Teheran, and Ceylon. With the rank of lieut.-colonel he was officer-in-charge of the medical divisions of Indian and British hospitals and consultant to a wide area.

After the war he returned to St. Albans, but shortly afterwards gave up his practice to take up his post as consultant in geriatics at the St. Albans City and Hitchin Group of hospitals. He was a foundation member, and for the past year secretary, of the Medical Society for the Care of the Elderly.

An enthusiastic sportsman, Dr. Jameson was a keen and expert rider and he supported the Aldenham Harriers Hunt for over 20 years. He was medical officer to their point-to-point races, and to those of the Hertfordshire Hunt at Friar's Wash. Rock-climbing and mountaineering fascinated him, and only ten days before his death he had been rock-climbing in Wales with his eldest son. He was also a keen tennis player.

E. D. H. C. writes: "Jameson brought to his post as consultant physician in geriatrics at St. Albans and at Hitchin a definite and lively personality and outstanding organising ability. He had real sympathy for the needs of the sick, and I know that the general practitioners of the neighbourhood will feel the poorer for the loss of such a 'whole man' at such an early age."

In 1932 he married Joan Isabel Colthurst, who survives him with a daughter and two sons, the elder of whom is a medical student.

MATTHEW H. LOGG

M.D. Aberd.

Dr. M. H. Logg, senior physician and medical administrator of Grove Park Hospital, London, died on April 20 at the age of 56.

After graduating in 1921 at the university of his native city of Aberdeen, he became a house-physician at the Aberdeen Royal Infirmary, and in 1923 he proceeded to the degree of M.D. He came to London to specialise in tuberculosis work, and after holding a house-appointment at the Brompton Hospital he entered the service of the old Metropolitan Asylums Board at Colindale Hospital. In 1926 he was appointed to Grove Park.

His long tenure of office there was, in microcosm, the history of the tuberculosis service in London, to which he gave so much of his energies. He was particularly interested in the problem of pregnancy in the tuberculous patient. He contributed to many discussions on this topic, particularly at the British Tuberculosis Association, of which he was a founder-member; and he published a review of the subject in the *N.A.P.T. Bulletin* in 1946. His other writings included papers in our own columns on the use of para-aminosalicylic acid in pulmonary tuberculosis.

Dr. Logg leaves a widow.

Appointments

BARRETT, AILEEN V., M.B., B.SC. Glasg., D.OBST.: asst. M.O., area No. 4, Middlesex.

FISHER, DOREEN M., M.B.: asst. county M.O. and school M.O., West Riding of Yorkshire (Batley and Heckmondwike).

FITZPATRICK, R. H. P., M.R.C.S., D.A.: consultant anæsthetist, Sidcup and Swanley H.M.C. group.

FLINT, F. J., M.A., D.M. Oxfd, M.R.C.P.: consultant physician, Sheffield No. 1 H.M.C. group.

FRY, E. N. S., M.B. Edin., D.A.: consultant anæsthetist, Tees-side H.M.C. group.

HAGAN, J. G., M.B.N.U.I., D.P.H.: deputy M.O.H. and deputy principal school M.O., Northampton county borough.

HICKEY, J. B., M.B.N.U.I.: registrar in ophthalmology, Norfolk and Norwich Hospital.

JOHNSTON, N. G., M.B. St. And., D.A.: consultant anæsthetist, W. Durham H.M.C., Bishop Auckland General Hospital.

KOTOWSKI, JAROSLAW, M.B. Polish School of Medicine, Edinburgh; senior casualty officer, Barry Accident Hospital.

MACGILLIVRAY, R. C., M.B. Edin., F.R.F.P.S., D.P.M.: consultant psychiatrist, Little Plumstead Hospital.

SANDFORD, F. M., M.R.C.S., D.A.: consultant anæsthetist, Dartford H.M.C. group.

ZAHORSKI, EDWARD, M.D. Warsaw: asst. orthopædic surgeon, London Road Hospital, Boston.

Diary of the Week

MAY 2 TO MAY 8

Monday, 3rd

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.12
4 P.M. Dr. Edwin Clarke: Cervical Spondylosis with Cord Compression.

INSTITUTE OF CARDIOLOGY, National Heart Hospital, Westmoreland Street, W.1
9.30 A.M. Dr. K. W. Donald: Exercise in Heart-disease.

INSTITUTE OF CHILD HEALTH, The Hospital for Sick Children, Great Ormond Street, W.C.1
5 P.M. Prof. G. Frontali (Rome): Proteins in Child Nutrition.

INSTITUTE OF NEUROLOGY, The National Hospital, Queen Square, W.C.1
5 P.M. Prof. Klaus Conrad (Homburg-Saar): New Problems of Aphasia.

Tuesday, 4th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
3.45 P.M. Prof. M. F. Lucas Keene: Development of the Pharynx. (Arnott demonstration.)

INSTITUTE OF DERMATOLOGY, St. John's Hospital, Lisle Street, W.C.2
5.30 P.M. Dr. E. J. Moynahan: Urticaria.

INSTITUTE OF NEUROLOGY
5 P.M. Dr. I. Wickbom (Sweden): Choice of Encephalography or Ventriculography for Examination of Intracranial Tumours.

WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY, St. Mary's Hospital Medical School, W.2
5 P.M. Sir Wilfred Fish: Dental Research in the Inoculation Department.

Wednesday, 5th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M. Dr. Martin Bodian: Hirschsprung's Disease and Chronic Constipation in Childhood.

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
5.15 P.M. *Section of History of Medicine.* Sir Charles Dodds, F.R.S.: Christopher Merritt (1614–1695), First Harveian Librarian. Mr. J. B. Oldham: Two Eighteenth-century Liverpool Surgeons—Park and Alanson.

INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. H. Haber: Lichen Planus and Lichenoid Eruptions.

MANCHESTER MEDICAL SOCIETY
4.15 P.M. (Medical School, University of Manchester.) Sir Heneage Ogilvie: Future of Surgery.

UNIVERSITY OF EDINBURGH
5 P.M. (University New Buildings, Teviot Place.) Prof. Henry K. Beecher (Harvard): Resuscitation and other Early Care of the Severely Wounded Man. (Macarthur lecture.)

MEDICO-CHIRURGICAL SOCIETY OF EDINBURGH
8.30 P.M. (18, Nicolson Street, Edinburgh.) Dr. A. G. Cruikshank Prescribing in General Practice.

Thursday, 6th

ROYAL COLLEGE OF SURGEONS
3.45 P.M. Prof. G. W. Causey: Sterno-mastoid Muscle. (Arnott demonstration.)
5.30 P.M. Prof. G. A. G. Mitchell: Sympathetic Nervous System in Relation to Throat, Nose, and Ear.

INSTITUTE OF CARDIOLOGY
9.30 A.M. Dr. Maurice Sokolow (California): Quinidine Therapy.

UNIVERSITY OF EDINBURGH
5 P.M. Prof. Gerhard Domagk (Wuppertal-Elberfeld): Chemotherapy in Tuberculosis.

Friday, 7th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M. Mr. E. T. C. Milligan: Surgery of Anal Canal and Fistula-in-ano.
4 P.M. Dr. Henry Miller: Allergic Disorders of Nervous System.

ROYAL SOCIETY OF MEDICINE
10.30 A.M. *Section of Otology.* Dr. J. C. Seymour: Circulation of Cochlea. Wing-Commander P. F. King: Psychogenic Deafness.
2.30 P.M. *Section of Laryngology.* Mr. Dudley Ashcroft, Dr. A. L. Peeney: Management of Hæmorrhage after Tonsillectomy.
5.30 P.M. *Section of Anæsthetics.* Dr. J. J. Bonica (Washington): Rôle of Anæsthetist in Management of Intractable Pain. Dr. E. H. Seward: Wasp Venoms and Anæsthesia.

INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. M. S. Thomson: Lichen Planus.

Saturday, 8th

SOUTH EAST METROPOLITAN REGIONAL TUBERCULOSIS SOCIETY
11 A.M. (Preston Hall, Maidstone, Kent.) Dr. A. Stocker (Illinois): Preferences in Surgery for Tuberculosis.

MIDLAND TUBERCULOSIS SOCIETY
11 A.M. (Cheshire Joint Sanatorium, Loggerheads, Market Drayton, Salop.) (Joint meeting with North-Western Tuberculosis Society.) Dr. E. Snell, Dr. R. Walshaw, Dr. L. A. McDowell, Dr. George Luntz: What is the Place, if any, of Mass Radiography.
2.15 P.M. Dr. Clark Penman, Dr. T. W. Lloyd, Dr. G. S. Erwin, Dr. V. Cotton Cornwall: Analysis of Place of Artificial Pneumothorax in Treatment of Pulmonary Tuberculosis.

Births, Marriages, and Deaths

MARRIAGES

ZEITLINE—ROBERTS.—On April 2, at the Paddington Registry Office, Dr. L. L. B. Zeitline, of 16, Norfolk Place, Hyde Park, W.2, and Miss Jane Roberts, of 30A, Sussex Place, Hyde Park, W.2.

Notes and News

EMPIRE RHEUMATISM COUNCIL

IN his report to the annual meeting of the Empire Rheumatism Council on April 28, Dr. W. S. C. Copeman, the chairman, paid tribute to the work of his predecessor, Lord Horder, who had held office since the inception of the Council in 1936. During the year a chair of rheumatology, the first of its kind in the Commonwealth, had been founded by the Council at Manchester University; and Dr. J. H. Kellgren had been appointed to this chair. In May, 1953, a medical deputation had been sent to the Minister of Health, in order to obtain a statement of future policy, and to secure Ministerial recognition of rheumatology as a specialty within general medicine.

Research activities continued to absorb the major part of the Council's slender financial resources. Work by Mr. A. A. Henly, PH.D., at the Hospital of St. John and St. Elizabeth, London, suggested that in rheumatoid arthritis such changes in steroid metabolism as were found resulted from metabolic abnormalities associated with the disease process, and that primary adrenal dysfunction was not a causative factor in its development. Among other research projects one on the long-term treatment of rheumatoid arthritis, carried out by Dr. J. M. Tweed at the West London Hospital, was made possible by a Philip Gray fellowship founded by the Shell Petroleum Company. Two E.R.C. fellowships for specific researches had been awarded. One fellow, Dr. J. K. Norymberski, working at the chemical research laboratory of the Sheffield Centre for the Investigation and Treatment of Rheumatic Diseases, had developed an analytical method for the simultaneous determination of formaldehydogenic and 17-ketogenic steroids, and a routine procedure for the estimation of the latter in urine.

The financial report reveals a total income in 1952–53 of £10,019 (exclusive of legacies), compared with £13,453 in the previous year. Medical expenditure was £8127, compared with £7220 in the previous year.

University of London

Dr. J. W. Landells, senior lecturer in pathology at London Hospital Medical College, has been appointed to the university readership in morbid anatomy at the college.

On March 24 the degree of M.D. was awarded to B. W. Lacey.

Ciba Foundation

Sir Macfarlane Burnet, F.R.S., director of the Walter and Eliza Hall Institute of Medical Research at Melbourne, will deliver a lecture at 5 P.M. on Tuesday, May 11, at 26, Portland Place, London, W.1, on the Problem of Virulence in Virus Disease.

Medical Women's Federation

The annual general meeting of this federation will be held on Thursday, May 6, at 8.15 P.M., at the Grand Hotel, Sheffield, when Dr. Annis Gillie will give a presidential address on Motive and Momentum.

Tribute to Dr. Thomas Anderson

A company of fifty attended a dinner held at Ruchill Fever Hospital, Glasgow, on April 20, to celebrate the 25th anniversary of the date when Dr. Thomas Anderson, now reader in infectious diseases in the university, joined the staff of Ruchill Sanatorium. Dr. James Lawson, medical superintendent of the hospital, presided. Prof. James Howie, proposing Dr. Anderson's health, remarked that his "powerful and successful resolve to upgrade the practice of infectious diseases was and is one of the real attractions of being a bacteriologist in the city of Glasgow." Professor Howie continued:

"Sometimes people say: 'Where are the great characters now?' The answer is that they have a different and a more difficult function to perform. Many of the great characters of the past were great dictators. Nowadays dictators are out of fashion. A great dictator in British medicine today would achieve only a great fall. Great achievement is harder today; it requires the patient man, the man who is able to sense the pace at which he can work the complex, still imperfect, still new, machinery of the health service. Our Dr. Anderson is one of these. His objectives are right, his ideals are high and unselfish, and he has a limitless capacity to hold on and to pull long and steadily in the right direction. Such qualities are less obvious and less spectacular than the fireworks of a great dictator. But the results may well prove to be equally valuable and perhaps of longer duration."

Gifts were presented to Dr. Anderson and to Mrs. Anderson, whose health was proposed by Dr. Peter McKenzie.

Royal College of Obstetricians and Gynæcologists

At a recent examination for the diploma in obstetrics the following were successful:

Pauline A. Adams, D. A. Aiken, D. J. M. Allan, N. J. W. Allan, G. A. Ames, W. M. Anderson, Liselotte Asch, Swayamprabha Bajpai, G. S. Banwell, D. W. Barnes, Rosalind A. Barnes, Margaret N. Barr, Mary M. Baxter, Jean M. Beecroft, Elspeth V. Beveridge, J. C. H. Bird, W. P. Black, A. S. Blake, Richard Blight, M. L. Bloom, F. P. Brown, J. W. Browning, Hilda M. Brunt, Marjory M. Buchanan, A. M. Burnford, Nancy I. Cardno, Kim Choy Chong, Marjorie Coates, Arnold Cohen, T. I. Cope, C. E. Cosgrove, Mary G. Coyle, Audrey N. Crocker, Kusum Amerchand Dalal, Charles Dansie, Alan Davies, Jean M. Davies, J. I. W. Davies, Joan V. Davis, G. B. Davison, V. E. Dean, J. Y. N. Devine, J. J. Devine, R. D. F. Druitt, Bernard Dudley, Domnal Duffin, John Dunlop, C. P. E. Elliott-Binns, J. J. Enright, D. L. Evans, Mary E. L. Evans, Jeannette G. Eveson, M. A. Fenton, Isabella C. Ferguson, Jack Fine, Alison M. Fleming, Margaret B. Fox, Mary U. Franklen-Evans, J. A. Girling, Ivan Goldman, J. H. Goode, P. M. Goodrich, P. D. Grant, Elizabeth D. Grassie, Hilary A. Hagan, Elizabeth M. Haines, C. J. J. Herlihy, K. M. Hewitt, Frances M. Hill, Sheila H. Hoey, Catharine E. Hollman, J. M. H. Hopper, John Houston, Edmund Howarth, T. M. Howell, D. C. Hudson, Doreen R. Hyder, Sylvia R. Ingold, Harry Jackson, R. F. Jackson, Lelia Jennings, I. M. Johnstone, Karthigesu Kanagsingam, D. P. J. Kelleher, E. I. Kohorn, Koussa Tadros Koussa, S. R. S. Laing, J. S. P. Lane, June P. Lawson, W. R. Lee, P. A. Lowe, Gwladys N. McCoach, J. Q. McCubbin, Jill MacDonald, Margaret R. MacD. McGilvary, Catriona D. McLeod, R. N. Malins, C. F. R. Mallett, G. C. Mansfield, John Manuel, Patricia L. Martin, C. J. G. Menzies, Barbara I. Miller, J. S. M. Mitchelson, I. A. Moollan, Donalda M. Morgan, Mavis H. Mortimer, A. L. I. Murphy, Rathindra Nath Nag, T. M. O'Brien, J. F. O'Kelly, E. G. Old, Chiew Seng Oon, Elspeth M. Orr, Margaret O'Sullivan, D. N. H. Owen, N. S. Painter, C. E. Parr, K. C. Parsons, Dina Patuck, Harrihar J. B. Pershad, William Peter, C. D. Peters, P. B. Poole, Sylvia E. Prebble, J. F. Preece, W. E. B. Preston, D. S. Ractliffe, T. F. Regan, Jean E. Ritchie, Kathleen M. Robb, T. E. Roberts, K. F. Robinson, Patricia M. Russell, Iqbal Sahney, J. F. Scarlett, Roy Schofield, Albert Schutz, F. G. M. Seager, Janet Shaw, R. G. Sinclair, G. D. Smellie, Janet U. A. Smith, S. A. Smith, Carol M. S. Spence, T. J. Stanton, Mary J. Starbuck, J. K. Steel, Michael Steele, D. H. Stewart, I. A. Stewart, W. M. B. Strangeways, Mary W. Sturges, J. S. V. Surman, Muriel M. H. Sutcliffe, W. R. Swaffield, G. S. Tapsall, M. K. Thompson, N. A. Toes, Dorothy I. Troup, A. G. Turner, Sam Vakil, M. H. Vickery, J. de M. Vink, P. O. Wakelin, Phyllis M. Wallington, D. G. Walker, A. G. Wallace, I. H. Watson, Josephine P. Werren, Susanne M. Williams, A. C. Wilson, D. G. Wilson, G. C. Winch, Hazel G. Wiseman, K. A. Wood, D. W. B. Woolven, E. G. B. Worthington, A. P. Wright, M. A. Young.

Radcliffe Infirmary

Lord Nuffield has given £15,000 to provide an operating-theatre for the Nuffield professor of surgery.

Poliomyelitis Vaccine

The National Foundation for Infantile Paralysis has given its approval for the start of the poliomyelitis vaccine trial in the U.S.A. (*Times*, April 27). The first inoculations were given to children in Virginia and Alabama on April 26.

Welfare of Handicapped Children

The National Committee for the Defence of Children is holding a conference on this subject at Church House, Westminster, on Saturday, May 8, at 2.30 P.M. Further information may be had from the secretary of the committee, Dr. Simon Yudkin, 23, Tillingbourne Gardens, London, N.3.

Varrier-Jones Lecture

Dr. Harold G. Trimble, associate professor of clinical medicine at Stanford University, California, will give this lecture at 26, Portland Place, London, W.1, on Friday, May 14, at 5 P.M. He has chosen as his subject Current Therapy in Pulmonary Tuberculosis.

Lebanon Hospital for Mental and Nervous Disorders

The annual meeting of this hospital will be held on Friday, May 7, at 5 P.M., at the Cora Hotel, Upper Woburn Place, London, W.C.1. The speakers will include Prof. Alexander Kennedy, F.R.C.P., and Dr. Alfred Torrie.

Rockefeller Grants

The grants to British organisations announced this week by the Rockefeller Foundation of New York include one of $125,000 to the Medical Research Council for fellowships in the medical sciences. This grant assures the continuance of the M.R.C.'s programme for travelling postgraduate fellowships until 1959.

The Fever Nurse

The general-trained nurse is allowed to take her training to qualify as a fever nurse in one year instead of the usual two years. Her training allowance has been amended (N.M.C. circular no. 36), and in future she will receive for the year £335 (the usual second-year allowance) instead of £320 (the first-year allowance).

Dr. Dennis Geffen is visiting Greece, Cyprus, and Turkey on behalf of the British Council.